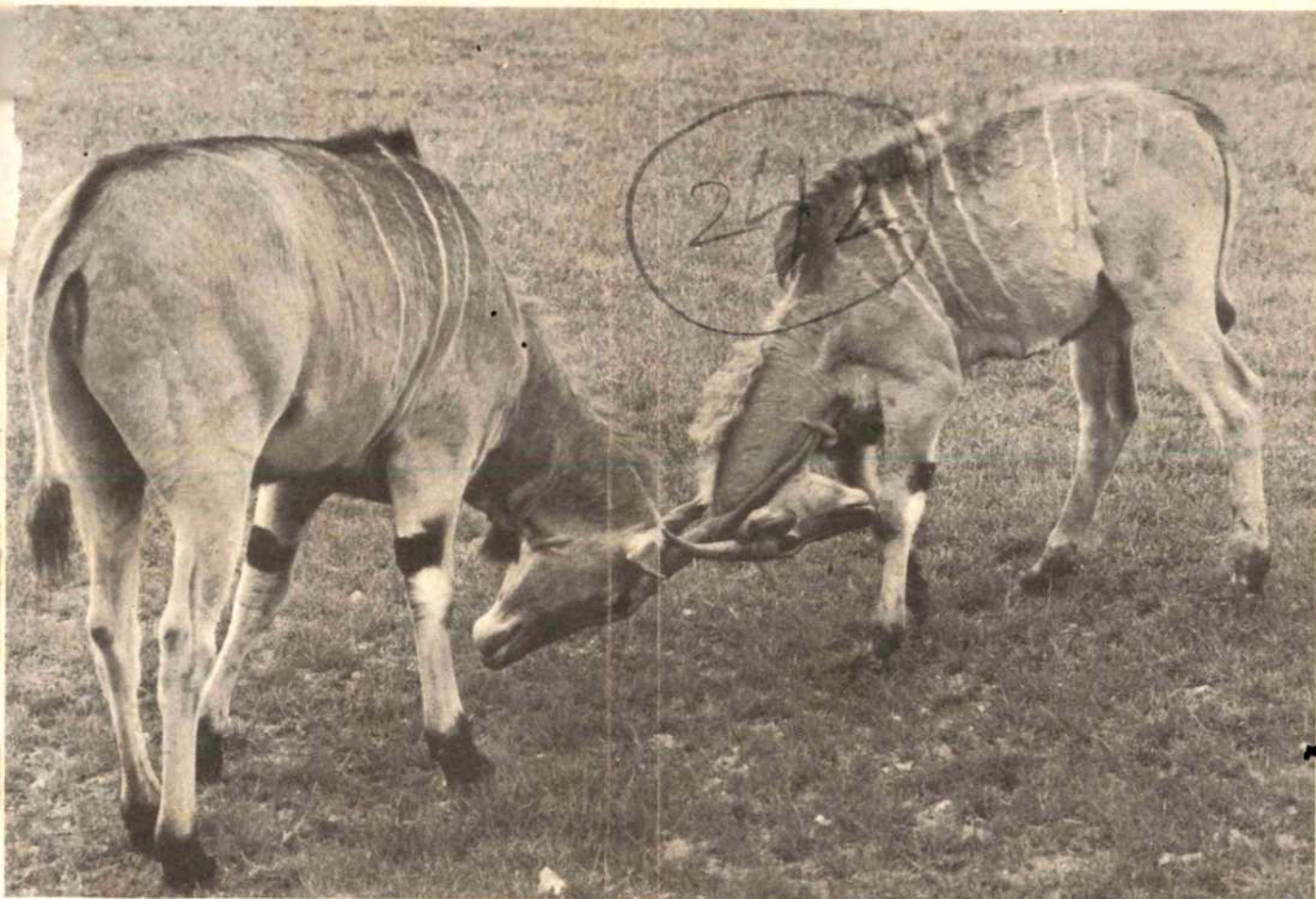


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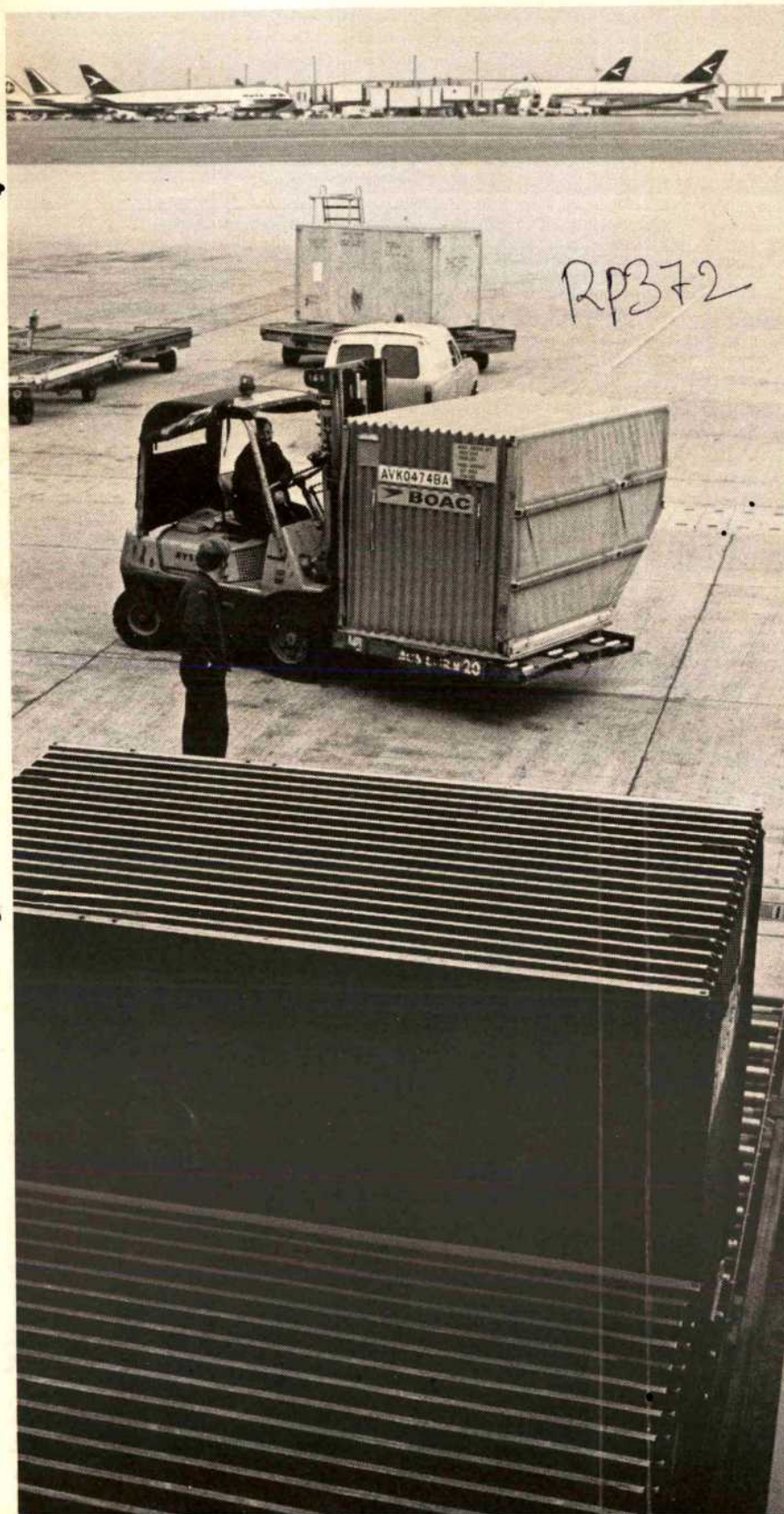
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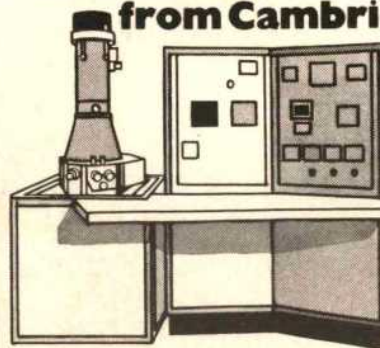
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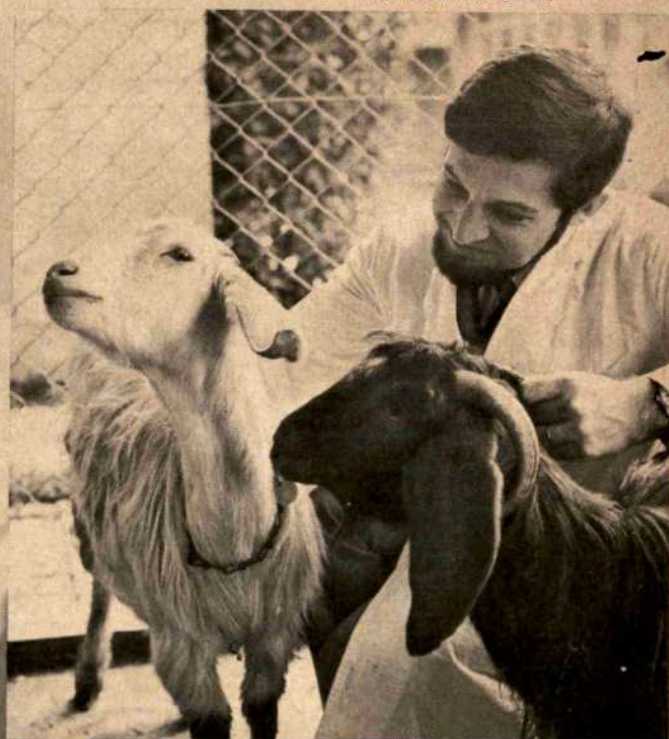
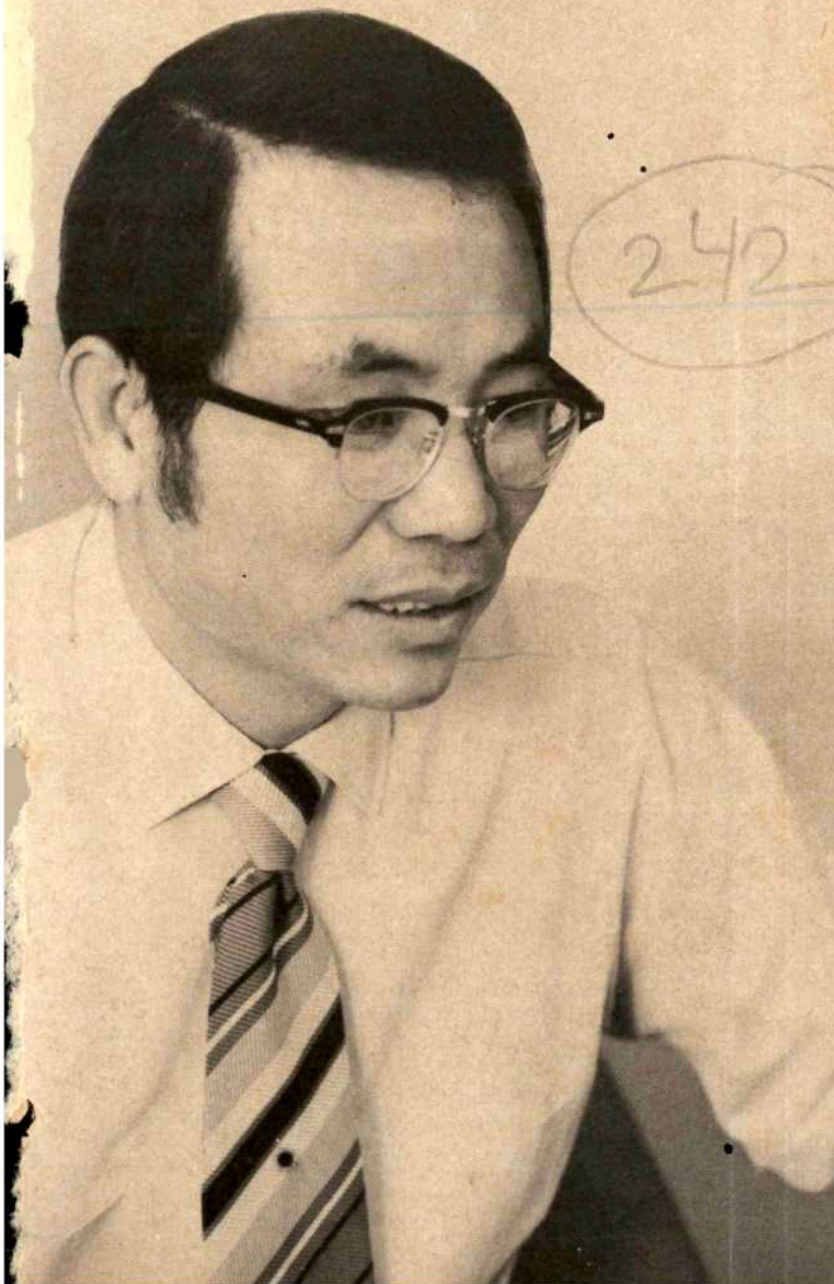


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	Page		Page
Should Science Proceed Uncontrolled?	1	Meteorites—Are large time differences in formation real?—CAMERON (Harvard College Observatory/Smithsonian Astrophysical Observatory)	30
Physics Award for Tunnelling Research	2	Palaeomagnetism—Post-depositional remanent magnetisation in deep-sea sediment—KENT (Lamont-Doherty Geological Observatory)	32
Recognition for Organometallic Chemistry	3	Polymer science—Flocculation of latices—EVANS and NAPPER (Sydney)	34
Short Notes	4		
NEW WORLD			
A Special Case for DDT Treatment?/Boll Weevil/Technology Assessment/Mariner 10	5		
NEWS AND VIEWS			
Does Zodiacal Light Intensity Vary?/New Look at Chromatin / Medical Radiology / Pharmaceutics / Cell Biology/Cell Biology/Theoretical Chemistry/Jupiter/Petrology/Super-conductivity/Nuclear Physics	7		
ARTICLES			
The Logic of Animal Conflict—MAYNARD SMITH (Sussex) and PRICE (University College, London)	15		
Geophysics—Ocean ridge spreading and sea level changes—HAYS and PITMAN (Columbia)	18		
Genetic code—Possibilities for its evolution from a preceding form—JUKES (California, Berkeley)	22		
LETTERS TO NATURE			
Physical Sciences			
Zodiacal light—Satellite observations of intensity variations—LEVASSEUR and BLAMONT (CNRS, Verrières le Buisson)	26		
Galaxy—Twenty-seven 'new' supernova remnants—CLARK (Sydney), CASWELL (CSIRO, Epping, NSW) and GREEN (Max-Planck Bonn)	28		
		Biological Sciences	
		Mouse genetics—Differences in conformational changes of albumin in <i>Mus musculus</i> —WILCOX (Indiana State)	35
		Platelet contraction—Regulation in an isometric system—COHEN and DE VRIES (Tel Aviv University Medical School)	36
		Teratology—Malformation in offspring from gonadotrophin-induced ovulations—ELBLING (Vienna)	37
		Airborne particles—Identification of human skin—CLARK and SHIRLEY (MRC, Hampstead, London)	39
		Photosynthesis—Environmental control of photosynthetic options in plants capable of crassulacean acid metabolism—OSMOND, ALLAWAY and SUTTON (Australian National University), TROUGHTON (Lower Hutt, New Zealand), QUEIROZ (CNRS, Gif-sur-Yvette) and LÜTTGE and WINTER (Technischen Hochschule, Darmstadt)	41

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 9 to 13

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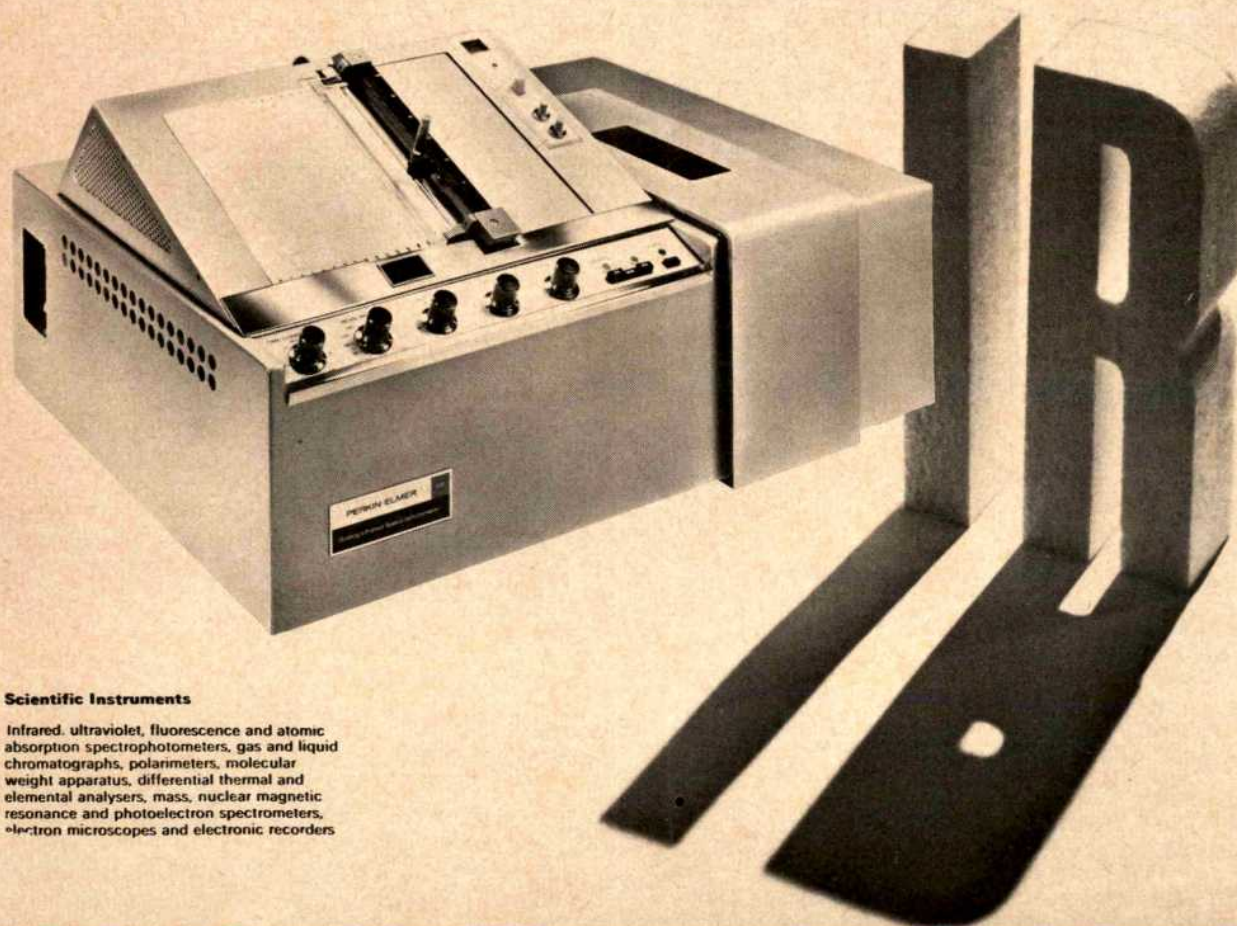
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	Page		Page
Seed germination —Accelerated by osmotic treatment— HEYDECKER, HIGGINS and GULLIVER (Nottingham)	42	Advanced Immunochemistry, Eugene D. Day (C. A. KING)	49
Neoformation — <i>In vitro</i> flower, bud, root and callus differentiation from excised epidermal tissues— TRAN THANH VAN (CNRS, Gif-sur-Yvette)	44	Determination of Sequences in RNA, G. G. Brownlee; Nucleic Acid Sequence Analysis, Stanley Mandel (M. SZEKELY)	49
Miocene hominoids —Locomotor affinities of tali from Kenya—WOOD (Middlesex Hospital Medical School, London)	45	The Constitution of Inorganic Compounds: Atomic Quantum Mechanics—Metals and Intermetallic Compounds, John L. T. Waugh (C. A. COULSON)	49
BOOK REVIEWS		The Visible Migration of Birds at Ottenby, Sweden, Carl Edellstam (editor) (G. V. T. MATTHEWS)	50
Evolution of Primates: An Introduction to the Biology of Man, A. B. Chiarelli (R. D. MARTIN)	47	The Optics of Rays, Wavefronts and Caustics, O. N. Stavroudis (JOHN MACDONALD)	50
Technological Planning and Social Futures, Erich Jantsch (C. FREEMAN)	48	CORRESPONDENCE	
Radiation Protection: a Guide for Scientists and Physicians, J. Shapiro (D. H. PEIRSON)	48	Misidentification or Misunderstanding? (D. A. C. Mills)	51
		Obituary —Professor Jean Hanson	51
		Announcements —University News	52

Next Monday's issue will include

- Pulsar**—p-n junctions in pulsar magnetospheres—HOLLOWAY (Cambridge)
- Geology**—Water solubility in basic and ultrabasic magmas—SCARFE (Alberta)
- Nickel**—Amorphous nickel produced by splat quenching—DAVIES, AUCOTE and HULL (Sheffield)

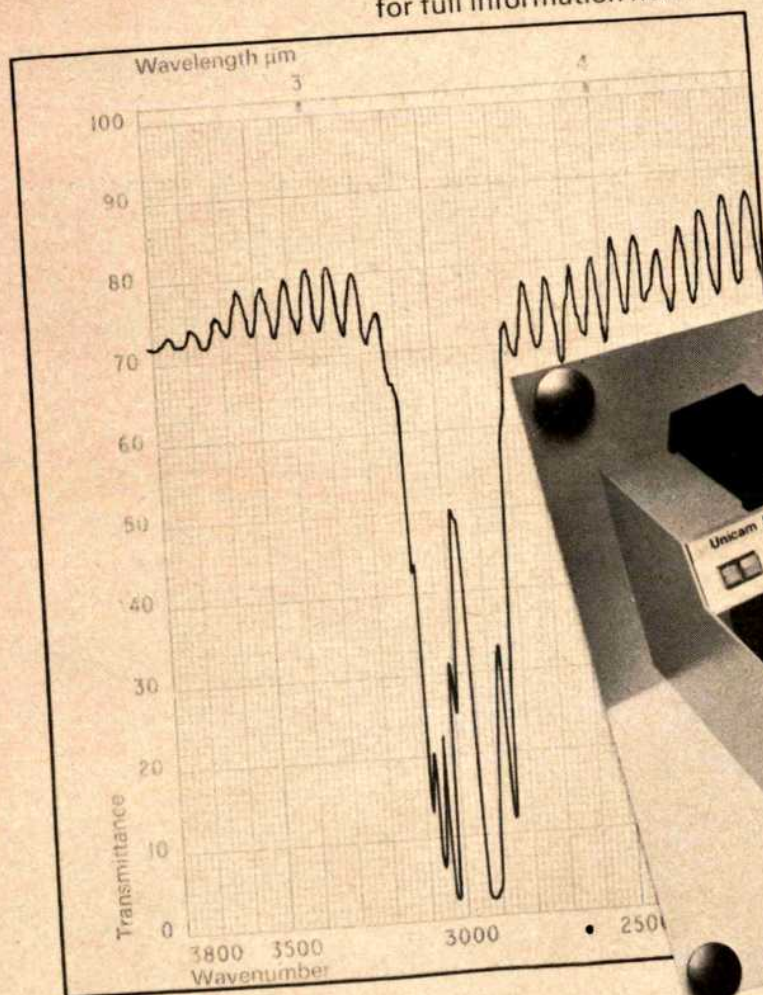
Next Wednesday's issue will include

- Endonuclease B**—Restriction endonuclease B and fl heteroduplex DNA—VOVIS, HORIUCHI, HARTMAN and ZINDER (Rockefeller University, New York)
- Poly(A)**—Synthesis *in vitro* by purified virions of VSV—PEREZ VILLARREAL and HOLLAND (California, San Diego)
- ²⁵³**Einsteinium**—Affinity for tumour tissue—HAYES, RAFTER, WASHBURH and BYRD (Oak Ridge)
- Fate mapping**—Fate map of larval organs of *Drosophila* differs from the map derived from embryological studies—FALK, OREVI and MENZL (Hebrew University, Jerusalem)

Official Notices

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See forward

Should Science Proceed Uncontrolled?

SCIENCE, as Peter Medawar put it, is the art of the soluble. Scientists do not venture forth into schemes of research without some indication that they will ultimately be successful in their work. This generally means two things: that their research must be completed in a reasonable amount of time by a reasonable number of people, and that it will not involve too many steps into the unknown at once. It is foolish to attempt to carry out jobs for which there is a serious lack of tools, experimental, mathematical or conceptual. Most research workers find it enough of a struggle to extend the capabilities of, say, electron microscopy without simultaneously looking for a digital computer that is a thousand times bigger than any existing at present and developing for themselves a mathematical framework within which to work. Research thus tends to be timely, not only in the sense of answering present needs, but in the sense of being appropriate to the competence of the times in which it is set.

This unromantic view of science—a view which nonetheless does not exclude or belittle the Newtons and Einsteins—raises an interesting question. Scientists in some sense regulate themselves by going for the soluble—the only way to remain sane and relatively satisfied. Science itself, however, has no comparable regulatory process to ensure that its growth is along the right lines.

Many would argue, of course that talking about right lines at all is a nonsense. Science, they would say, is what scientists care to make it by their research, and it is nobody's business to organise other people's labours in order to cause science to develop along the lines of some personally conceived grand scheme. Certainly one cannot but have sympathy with those subjected to Five Year Plans, Global Strategies, Milestones and other orderly ideas imposed on some branches of science that have been blessed with tidy-minded bureaucracy at the top. Such rigidity often seems to discount creativity in science and to equate a healthy science solely with one in which there are enough data to go round. Nevertheless the excesses of regulatory zeal manifested in certain places should not detract from the need to ask the question whether the development of science should be entirely freed of controls. Every year universities turn out hundreds of PhDs, possessing, in theory, the skills and qualifications to do scientific research. If their work comes within the sphere of influence of the customer/contractor relationship they will experience certain forces which bear some resemblance to market-place economics and they cannot afford to be too cavalier in their disregard of the customer even though he may not have a very clear idea of what he wants, only of what he can afford. If, on the other hand, they can stay in some university department into which the customer has not yet ventured they can be free of many external forces that might seek to dictate the content of their research. Anything that is soluble is permissible.

It may be objected that the peer review process prevents excesses from happening. Research work comes under

formal scrutiny by grant-giving bodies before it is started and again by the referees of learned journals when it is completed. It comes under more informal review in the continuous circulation of scientists around the community. Is this not adequate control? The difficulty with the peer review process is that it only affords the reviewer a very limited view of the science, as opposed to the scientist, and ultimately his answer must be yes or no. He may wish to say that the applicant be encouraged to work on a different problem. He may wish to have the perspective of seeing who else is applying, in order to ensure that money is most effectively spent. He may even, if sufficiently energetic, wonder about how the proposed work compares with proposals being made in other countries, since science supposedly transcends national frontiers. But how often is it possible to do anything about these broader issues? Likewise referees are frequently faced with manuscripts which are impeccable but which, if published, will be neither read nor used. The dilemma seems always to be that of being thought arrogant if one speaks one's mind and stands up for a particular view of the development of science. Yet, privately, scientists can regularly be heard to bemoan the way in which bandwagons are followed to the detriment of less spectacular, but very necessary, research, students are encouraged to move into already overcrowded fields and so on.

It is asking a lot of administrations for them to define guidelines for scientific as opposed to administrative direction. It is better that practising scientists—unfortunately the very ones who can least spare time from their research activities—should be deeply involved. Money for scientific research is not going to flow ever more freely in the future and scientists must ensure that their opinions are heard now about the way in which science should develop rather than risk having administrative and political solutions imposed on them from above.

100 Years Ago



MR. JAMES DALLAS, of Benakandy, Cachar, writing us on the subject of inherited peculiarities, says that a friend of his has a black-and-tan English terrier dog, two inches of the end of whose tail is folded back so acutely as to come in contact with the upper portion. A pup, of which the dog is the undoubted father, has inherited the paternal peculiarity, with the difference that, instead of the end of the tail being turned up, it is turned down.

NOBEL PRIZES

Physics Award for Tunnelling Research



Dr. Brian Josephson, a particularly young winner of the Nobel Prize.

THIS year's award of the Nobel Prize for Physics to Leo Esaki, Ivor Giaever and Brian Josephson recognises the importance of tunnelling phenomena in semiconductors and superconductors. According to the quantum theory, electrons have a small probability of tunnelling through a potential barrier which is impenetrable according to classical theory. The phenomena depend on this probability.

Semi-conductors or super-conductors

The tunnel diode, discovered by Esaki (University of Tokyo) in 1957, is a p-n junction in a semiconductor so heavily doped that both sides are degenerate. The space-charge layer in the junction forms the potential barrier. When a small voltage is applied to bias the junction in the forward direction electrons tunnel from the n side to the valence band on the p side. When the bias voltage is sufficiently great, however, the electrons on the n side will have energies within the energy gap on the p side; since there will be no allowed states to receive the electrons, the current will drop and the diode will have a negative resistance. When the forward bias is sufficiently large the electrons will be able to tunnel across to the conduction band on the p side, and the resistance will become positive again. These properties of the diode enable it to be used in high speed amplifiers and oscillators. Since the electron current is affected by other excitations in the semiconductor, the diode can be also used to study these

excitations.

Giaever, originally Norwegian and a mechanical engineer, switched to physics on joining the General Electric Research Laboratory, New York. Impressed by the analogy with semiconductors, he used tunnelling to study the superconducting energy gap. In this case, the potential barrier was an insulating layer (usually an oxide) sandwiched between two metals. If one metal is normal and one superconducting (the NIS sandwich) and if the temperature is low, electrons will be able to tunnel from normal metal to superconductor only if the voltage bias is sufficient to carry them over the gap. In 1960 Giaever announced the first observation of the energy gap by this method. Giaever also realised that there is an analogy between the superconductor/insulator/superconductor sandwich and the tunnel diode and that the former should, under suitable conditions, also have a negative resistance characteristic. This he observed and the effect is now being developed in devices. A fuller account of Giaever's discovery has been given by Schmitt in *Physics Today* (14, 38; 1961).

Subsequent theoretical work showed that the characteristic of the NIS sandwich provides a direct measure of the density of electronic states of a superconductor. Because of the effect of other excitations, notably the phonons, on the density of states the tunnelling characteristic can be used to study these other properties. This has helped to confirm the basic theory of superconductivity as well as to yield important information on the phonon spectra of superconductors.

Tunnelling Supercurrents

In 1962, in a two-page letter to *Physics Letters*, Josephson (University of Cambridge), then aged twenty-two, predicted that it would be possible for supercurrents to tunnel between superconductors and that this tunnelling would be accompanied by a number of interesting effects. Essentially, Josephson showed that the whole superconducting sandwich was a single superconductor governed by a single wave

function, and that there were low-lying many-electron states that carried small currents without dissipation. If a large current passed through the sandwich, a voltage V would appear across it and there would be a non-dissipative contribution to the electric current oscillating at the frequency $2eV/h$ independent of the material. If such a junction is placed in a microwave field, this supercurrent leads to steps in the current-voltage characteristic. Josephson also stated (and showed in detail in later papers) that a magnetic field would modulate the phase of the wave function across the junction in a way analogous to that in which the phase of a light wave depends on path length. The result is that the dependence of the maximum Josephson supercurrent through a junction on magnetic field produces a 'Fresnel diffraction pattern'. The story of Josephson's discovery has been told by Anderson in *Physics Today* (23, 23; 1970).

At the time John Bardeen was sceptical that the effect would be as large as Josephson predicted. At an international conference in 1962 there occurred one of those historic moments in physics, the young Josephson defending his theory against the doubts of the 'elder statesman'. Within a few months, experiment had vindicated Josephson.

Since that time many beautiful experiments have been performed that demonstrate the effects of a magnetic field on Josephson tunnelling and which show that the phase of a superconducting wave function is coherent over macroscopic distances (at least of the order of centimetres). The effect is the basis of sensitive devices for measuring magnetic fields, voltages and small currents, and junctions are under development as computer elements.

The a.c. Josephson effect has been detected and used to provide the most accurate value of the fundamental constant e/h ; this, in turn, has led to a reassessment of the values of the other fundamental constants. It is also used to provide a new voltage standard and is being developed for the generation, detection and mixing of electromagnetic waves.

Professor G. Rickayzen of the University of Kent at Canterbury describes the research work for which the Nobel Prize for Physics was awarded.

Recognition for Organometallic Chemistry

Professor P. L. Pauson of the University of Strathclyde summarises the work on organo-transition metal chemistry which has earned its two chief founders the 1973 Nobel Prize for Chemistry.

ERNST OTTO FISCHER and Geoffrey Wilkinson share this year's Nobel Prize for Chemistry for spearheading the spectacular advances in organo-transition metal chemistry during the past twenty years. Not only were they among the first to recognise in 1952 the unique structure of ferrocene but their success in synthesising other "metallocenes" and many related cyclopentadienyl-metal complexes opened up the whole field.

Sandwich Compounds

Wilkinson used the name "sandwich compounds" for the metallocenes to describe molecular architecture, a structure consisting of two parallel five-membered carbon rings (cyclopentadienyl groups) symmetrically arranged around the central metal atom. The rings may be regarded as having sextets of π electrons and the important consequence, the aromaticity of ferrocene, was recognised and demonstrated by R. B. Woodward. The extensive organic chemistry thus opened up continues to be widely explored, most intensively and successfully in A. N. Nesmeyanov's Moscow laboratory, whose recent work has revived interest in ferrocene derivatives as anti-anaemic agents. Despite some early commercial promise, for example, for vapour plating and as fuel additives—including anti-knock agents, where a cyclopentadienylmanganese compound has earned limited practical success—no major direct application has yet repaid the intense effort put into this field. Initially industrial interest was so strong that it was not uncommon for a new type of cyclopentadienyl complex to be synthesised independently in three industrial laboratories as well as in Fischer's and Wilkinson's laboratories. But the work of Fischer and Wilkinson gradually diverged as the field broadened.

Theoretical interest in these remarkable structures was no less intense than practical interest, and gradually deepening understanding helped greatly in extending the whole area of research. J. Chatt and L. A. Duncanson had taken an important step in 1953 by applying

M. J. S. Dewar's π -bonding ideas to explain the structure of the organometallic compound known longer than any other—Zeise's ethylene-platinum salt. The relationship to this and the cyclopentadienyl sandwiches of other known compounds, including some acetylene complexes first prepared by W. Reppe and his group as well as H. Reihlen's butadiene-iron complex, emerged gradually. During this period both Fischer and Wilkinson worked on a variety of related alkene, diene and triene complexes.



Professor Geoffrey Wilkinson

Suspicion that the most puzzling of the earlier discoveries, F. Hein's "polyphenylchromium" compounds, might also belong in the "sandwich" class received striking confirmation when E. O. Fischer and W. Hafner succeeded in synthesising the prototype: bisbenzene-chromium. With the impressive range of other arene-metal complexes subsequently synthesised in his laboratory, this will undoubtedly continue to be regarded as Fischer's most distinctive and important contribution.

More recently, most of his work has been concentrated on the intriguing carbene complexes, first prepared in his

laboratory as a result of a most skilful and purposeful search for suitable synthetic methods. These studies have taken him back much closer to the metal carbonyls, on which he worked as a student under W. Hieber, whom he succeeded in the chair of inorganic chemistry at the Technische Hochschule of Munich in 1964.

Fischer's entire scientific work to date has been done there and at the University of Munich (1957-64). He resisted calls to other chairs which would have taken him from his native city and further from the Alps which he loves and where he relaxes—usually in the company of his students, walking and skiing from an attractive chalet built with the proceeds of the bis-arene-chromium patents.

Return to Imperial College

Wilkinson—a Yorkshireman born in Todmorden—likewise holds office in his own alma mater, the Imperial College of Science and Technology, London. He returned there in 1956 after thirteen years in North America, having gone to Canada during the war to do radiochemical work in connection with the development of the atomic bomb and moving by way of California to the Massachusetts Institute of Technology and then Harvard.

Most of his "sandwich" work was carried out at Harvard where Al Cotton, co-author of his famous textbook, was the first student to work with him in this field. Among Wilkinson's contributions of that period, his use of the then quite new NMR techniques demonstrated their great potential in this field and led to later discoveries of many interesting aspects of the behaviour of organometallic molecules. Since returning to London, his interests have gradually moved to other areas, notably the transition metal alkyls (he has devised molecules of almost as surprising stability as the original "sandwiches") and catalysis (he found and studied some of the most active homogeneous hydrogenation catalysts).

It is in such catalytic aspects, and in the use as chemical intermediates of such metal complexes as Fischer's carbene derivatives, that greatest interest and promise of use resides at present; but regardless of future developments, this year's Nobel Laureates have added a remarkable chapter to chemical knowledge.

Short Notes

Mark V—A Sound Investment

DETAILS and engineering drawings for the Mark V "Jodrell Bank" radio telescope have now been sent out for tender. Tenders will be in early in January, 1974, said Professor Sir Bernard Lovell last week, and a decision on whether to go ahead with building the telescope will be made by the SRC next spring. Sir Bernard also said that the staff at Jodrell Bank are "very happy" with the final design, and he is confident that the high accuracy required for its construction can be achieved. Although the final decision on building the instrument cannot be made until tenders have been considered, there is an air of optimism at Jodrell Bank, engendered partly by the recent granting of formal planning permission to build the telescope in the Meifod valley.

Outside Manchester, there have been reports that this optimism might yet prove unfounded, since the SRC is at present considering two expensive astronomy projects, the Mark V and the Northern Hemisphere Optical Observatory (NHO). Opponents of the Mark V argue that if the SRC is forced to choose between these projects then the radio telescope is more likely to be axed, because of the rising cost of steel, many thousands of tons of which are needed in the construction of such an instrument. But that argument is a two-edged weapon; the Mark I telescope at Jodrell Bank is today worth more as scrap than it cost to build, and from that point of view, the Mark V is a more sound investment than the NHO. According to a spokesman for the SRC last week, however, both optical and radio astronomers can rest assured in the knowledge that "planning is proceeding on both these projects and there is no reason to suppose that a choice will have to be made".

BA Launches BASS

THE inaugural conference of the British Association Students' Section (BASS) next January is to be entitled 'The Social Responsibility of the Scientist within the Community' which is a fair summary of BASS's preoccupations, as it now sees them. Speakers will include not only Dr Magnus Pyke, secretary of the British Association, and Sir Peter Medawar but also Mr James Moorhouse, of Rio Tinto Zinc, who will put the industrialist's point of view.

The new section will be distinct from the British Association of Young Scientists (BAYS) and membership is not restricted to scientists or to members of universities. It will be chiefly concerned with the consequences of science rather than with acquainting the public with developments in science, which has

been one of the main objectives of the British Association itself.

The BASS plans to hold a yearly conference and to carry on year-round activities in local branches based on places of higher education. These will not attempt to compete with already established scientific societies in providing general lectures except in certain cases, such as the University of Exeter, where the scientific societies are felt to be inadequate; but they will be involved in projects decided at the previous conference. The projects may be on similar lines to those organised by the British Association proper—for example the study groups on the role of research in higher education, the ethics of biological research and so on. Certainly they will involve the collection and discovery of already available data rather than original scientific research, as there are no central funds available for branch activities. The BASS will provide for the first time a forum for student discussion of science-related topics at the national level; and its creation may mean a new lease of life for the British Association.

Drapes Off at the DoE

FOLLOWING the recommendations of the Select Committee on Science and Technology that government departments should give regular accounts of their research activities, the Department of the Environment has produced its first report on research and development (HMSO, £0.42). The report reveals that in 1973-74, a greater proportion of the department's research resources are to be devoted to planning and transportation, and to environmental pollution and resources, all at the expense of building and construction.

Research and Development in the Department of the Environment

	1972-73	1973-74*
	(£ million)	
Planning and transportation	4.9	10.3
Building and construction	7.2	8.4
Environmental pollution and resources	2.5	5.8
Other expenditure†	2.6	2.7
Total	17.2	27.2

* Planned programme.

† Includes grants-in-aid to research associations, the Centre for Environmental Studies and so on.

The expenditure involved is shown in the table, which reflects the transfer of funds from the Natural Environment Research Council according to the Rothschild recipe and from the Department of Trade and Industry. Much of the department's research effort is centred on its four research establishments—the Building Research Establishment, the Transport and Road Research Laboratory, the Hydraulics Re-

search Station and the Water Pollution Research Laboratory, which between them employ more than 1,400 scientists and engineers.

Soyuz-Apollo Project

THE second round of preparatory talks for the joint Soyuz-Apollo project (scheduled for 1975) was held in Moscow from October 1 to 18, 1973, and dealt with problems of flight ballistics, coordination of the Soviet and American control centres and problems of crew transfer between the craft. In connection with the latter topic, the Soviet team revealed full details of the cause of the Soyuz 11 disaster of June 30, 1971.

Although as early as July 4, 1971 a *Pravda* article by Academician Boris N. Petrov (a leading figure in the Soviet space programme) hinted at mechanical failure, and although it was later announced that the death of the three cosmonauts was caused by loss of cabin pressure on re-entry, the details remained a secret. Now, apparently on the insistence of the United States team, it has been revealed that the firing of twelve explosive bolts to disconnect the re-entry capsule from the orbiting craft was more violent than anticipated, and accidentally loosened a safety valve cap, thus triggering an exhaust valve, resulting in total loss of cabin pressure within 45 seconds.

Ground tests after the accident revealed that it would take 27 seconds to close the valve by hand—17 seconds longer than the crew could have remained conscious. Earlier Russian reports that two of the cosmonauts were found "with hand raised" would suggest that such an attempt was made. Like the fire in which three Apollo astronauts died, the Soyuz tragedy seems to have been caused by a 'safety' mechanism that could not be operated with sufficient speed. Also, like the American disaster, it has led to modifications of the craft, which were tested out by a space-suited two-man crew in the 2-day Soyuz 12 mission of September 1973.

What is a Quark?

In *Physics Reports* (8, 173; 1973) Lipkin quotes the following definition of a quark, from a standard German-English dictionary: Quark, m. curd, curds; slime, slush, filth; (fig.) trifle, rubbish, trash; (sl.) du verstehst einen—davon, you understand damn-all about it; den alten—aufrühren (fig.), stir up mud. -ig, adj. containing curds; dirty. -kase, m. soft or cream cheese.

This reminds one of the Prime Axiom of physics: everything is made up of smaller pieces. This, together with the Corollary (some of the pieces attract each other; some are repulsive), seems to sum up the subject adequately, although glossing over some details.

NEW WORLD

A Special Case for DDT Treatment?

by our Washington Correspondent

IN the past few years, bewhiskered caterpillars of the Douglas fir tussock moth have been quietly munching their way through nearly a million acres of fir forests in the north-western United States. The moth suddenly began a population boom in 1971, defied all predictions that the outbreak would end this year from natural causes, and is about to present the Environmental Protection Agency (EPA) with a serious dilemma. Should the ban on DDT, which was imposed last year after a long and bitter debate, be temporarily lifted so that the caterpillars can be sprayed when they hatch next spring? Last week, while American troops were on alert around the world and a domestic crisis was gripping the United States, a sub-committee of the House Agriculture Committee took time to hear about the caterpillars.

The moth is always present in the Pacific North-West, but it is usually relatively untroublesome, existing in small numbers in balance with its natural predators. Every so often, however, for reasons that have never been adequately explained, the moth undergoes an explosive population growth. Usually the epidemic suddenly ends in the third year, when the caterpillars all die off from a virus infection which spreads through the eggs during the winter months, and these periods of heavy infestation are then followed by several years of relative quiet. This time the moth refused to follow its traditional three-year cycle. According to the Forest Service, at the last count the insect had defoliated to some degree 657,000 acres in Oregon and Washington State and another 125,000 acres in Idaho. The committee was told last week that as many as 1.5 million acres of forests could be stripped next year if the infestation is not checked. The foresters in the area and the lumber companies that make their living from the trees want to kill the insects when they hatch next spring with the only pesticide they know will do the job—DDT. This does not appeal to environmentalist organisations which fought long and hard to get DDT banned, or the EPA which is understandably reluctant to allow use of a pesticide which it banned only a year ago amid a blast of publicity and a barrage of complaints from farmers, pesticide manufacturers and some scientists. The choice is, however, not

simply a matter of DDT or no DDT, and it is greatly complicated by the moth's failure during the past year to conform to its previous population trends.

To appreciate the basis of the EPA's dilemma, a little knowledge of the life cycle of the moth is required. Tiny tussock moth caterpillars hatch over a period of about a month in late May and early June from eggs laid during late August and September. The caterpillars go through five to seven moults, increasing in size as they eat first all the new foliage growth and then old foliage; they pupate in August and emerge in 10 to 18 days as adult moths. The female moth is wingless and mating takes place on the cocoon; she lays some 200 eggs in a mass and dies within a few weeks. The eggs remain on the trees during the winter and hatch in the spring. Thus, if the caterpillars are to be attacked with a pesticide, the application must come just as they first emerge, before they have had chance to start munching the foliage, and the pesticide should ideally remain active for a month or so to kill caterpillars that hatch late.

When a population explosion takes place, it usually goes undetected during

the first year, but becomes painfully obvious when caterpillars start stripping the trees in the second year. If left alone, the outbreak tends to end abruptly in the spring of the third year, because of the explosive spread of a nuclear polyhedrosis virus which kills off some of the caterpillars at the end of their first moult (instar). The infection spreads because the dying larvae infect foliage which is eaten by other caterpillars during their second instar, and so on—it is calculated that if 10% of the caterpillars are infected during their first instar, the entire population will be virtually wiped out by the end of June.

The problem is, however, that although the virus infection kills off the outbreak abruptly, it does not complete its work until a fair proportion of the caterpillars have survived long enough to munch foliage, and trees are still stripped even in the third year of an outbreak. The usual practice has thus been to spray infested trees with DDT in the spring of the third year of an outbreak but that was stopped in 1969, when the Department of Agriculture (the EPA was not then formed) banned the use of DDT on forest land.

The present outbreak began in 1971, and, by rights, should have ended

BOLL WEEVIL

An End in Sight

by our Washington Correspondent

WHILE a verbal battle was taking place in Washington last week over the use of DDT (see accompanying story), the US Department of Agriculture announced that it has successfully completed a programme which proves that it is technically possible to eradicate the boll weevil in the United States. One of the most destructive insect pests in the cotton fields, the boll weevil is now attacked with more insecticide than any other pest, and its elimination could save cotton farmers up to \$200 million a year in lost production.

The Department of Agriculture's announcement was based on the results of a two-year study of the use of integrated pest management techniques in a 5,000 square mile area in Mississippi, Alabama and Louisiana. The experiment involved the application of pesticides, the use of sex pheromones and, finally, the release of large numbers of sterile male insects. First, several limited pesticide applications were made in late

autumn to kill the last generation of weevils to reproduce that year, and to reduce the population which was due to hibernate during the winter. Then, in the spring, male sex pheromones were used to bait traps in and around the cotton fields (the boll weevil is one of the few species of insects where the male, and not the female, produces sex attractants). Finally, sterile males were released in the cotton fields in numbers far greater than those of the males that had survived the onslaught of pesticides the previous autumn.

Surveys conducted at the end of the second year of the experiment indicated that there was no evidence of boll weevils in 235 of the 236 cotton fields in the core of the experimental area. It should be pointed out, however, that it will be several years before the weevil can be eradicated by these techniques, because a national elimination plan must be formulated and approved by all the parties involved. Nevertheless, the experiment has raised hopes that one of the most destructive pests in the United States may at last be on the way out.

abruptly with a massive infection in June this year. Nevertheless, in March, the United States Forest Service and the States of Washington and Oregon petitioned the EPA to allow the use of DDT on the outbreak this spring. They wanted to use 200,000 pounds of the pesticide on about 500,000 acres of forests, to prevent third-year defoliation, and to make sure that the infestation did not spread any further.

The EPA sent a team of investigators to take a look at the area and they returned with the finding that the egg masses were contaminated with virus—albeit at a fairly low level—and their report said that there was every expectation that the population would collapse without the use of DDT. They did, however, allow the experimental use of four chemical alternatives to DDT—Zectran, Dylox, Sevin-4-oil, and Bioethanomethrin—and the testing of a polyhedrosis virus and the bacterium *Bacillus thuringiensis* against the caterpillars.

The virus infection has not worked. The moth spread to an area about twice that of the original infestation. There seems to be no explanation of why the virus failed to do its work, except for the possibility that it may not have been present in sufficiently high density to wipe out the population. As for the insecticides, all were moderately effective but not as good as DDT, and the microbial agents proved to be promising but they will not be available in sufficient quantities for use in a large outbreak.

An extensive survey is now being undertaken to examine the egg masses that have just been laid, to try to predict the course of the infestation next year. Some of the eggs will be hatched in laboratories next March, and that should give some indication of the chances of virus infection wiping the insects out next spring. If it seems that the population will collapse from virus infection, the EPA could again deny the use of DDT. But the repercussions of another wrong prediction are obvious. Alternatively, the agency could agree to the use of DDT to prevent final-year defoliation of the infested trees, but that would lay it open to charges from environmentalists that DDT was used in a situation that did not warrant it. Moreover, there is a fear that if the DDT ban is lifted in this case, the floodgates would be opened for special pleas in countless other cases.

The EPA has, in fact, already granted exemption from the DDT ban this year for the spraying of pea crops in Washington to kill pea leaf weevil. That decision was taken because no other pesticide was available, and it was used in a region where there is little water runoff or likelihood of damage to wildlife. Although the exemption from the

ban has not sparked off a rash of other formal requests to use DDT, a parade of witnesses before the House Agriculture Committee last week told of numerous cases in which they would love to break out the DDT spray.

The hearings themselves were concerned with a bill introduced by Congressman Mike McCormack, whose constituents in the state of Washington are up in arms about the EPA's handling of the matter. The bill would essentially force the administrator of the EPA to approve use of DDT whenever the Secretary of Agriculture requests it. In other words, it would strip the EPA of its control over DDT. Although the committee members who bothered to attend the hearings last week are in strong sympathy with the legislation—it would, after all, give the Agriculture Department, over which they are supposed to preside, more power—its chances of survival if it ever reaches the floor of the House are considered slim. It is unlikely that many congressmen would be willing to put such a sensitive matter back in the hands of a department so closely allied with the industry concerned.

If last week's hearings demonstrated one thing, it was that the emotion that surrounded the DDT debate has by no means diminished since the pesticide was banned. The committee room echoed to all the familiar arguments, emotive phrases and accusations of scientific malpractice that characterised the extensive public hearings on the matter last year. At least the committee staff showed what they thought of the proceedings. They spent most of the time reading magazines and newspapers while witnesses on both sides of the debate rehashed their arguments and congressmen asked a spate of naive questions.

TECHNOLOGY ASSESSMENT

Some Cash at Last

by our Washington Correspondent
THE Office of Technology Assessment (OTA) is in business at last, more than a year after Congress decided to set it up. The office, which will conduct analyses and offer advice to the legislative branch of the federal government on issues involving science and technology, has been given \$2 million to spend in the 8 months that now remain in the 1974 fiscal year. The money, which was contained in the Legislative Appropriations Bill, was delayed by a fight over an entirely unrelated matter (see *Nature*, 245, 284; 1973), but the holdup prevented the OTA from hiring staff, appointing a director or doing any work—in other words, the office existed in name only.

Although \$2 million is a good deal less than the \$5 million that the OTA's

backers were requesting for its first year of operation, the funds will allow a start to be made soon on a few specific problems, which will be tackled by *ad hoc* panels. The first move, however, will be for the OTA Board, which consists of six senators and six congressmen, and which is chaired by Senator Edward M. Kennedy, to appoint a full-time director for the office. Emilio Q. Daddario, a former congressman who was largely responsible for developing the legislation that led to the setting up of OTA, is expected to get the job early next month.

MARINER 10

Go for Take-off

by our Cosmology Correspondent

THE first spacecraft to use the gravity of one planet to help it on its way to another is due for launch on or about November 3. Mariner 10 will swing past Venus and on to Mercury, where the first encounter will take place around March 29, 1974. The spacecraft will, if all goes well, remain in a circum-solar orbit so that further encounters with Mercury will take place on September 22 and at roughly six-monthly intervals thereafter. The spacecraft should still be functioning for the second encounter, at least.

On the face of things the Venus observations form the more interesting part of the mission, since enough is now known about Venus to hint at a complex planet with slow retrograde spin, extensive cratering, and an active atmosphere. But so little is known about Mercury that any information from Mariner 10 will be invaluable. And at least Mercury is not obscured by cloud; two television cameras equipped with 150-cm Cassegrain telescopes will produce resolution of 1.5 km for the full coverage of the planet and 100 m for selected areas.

Apart from the television cameras Mariner 10 will carry six scientific experiments, including an infrared radiometer, an extreme ultraviolet experiment, a 'radio science' experiment, a magnetometer and two experiments to measure the solar wind (particularly inside the orbit of Venus) and the galactic cosmic radiation. The infrared experiments will, of course, provide estimates of the surface temperatures of both planets. On Mercury large temperature variations are to be expected, for a thin atmosphere (if there is one at all, a matter which should be settled by the ultraviolet measurements) will allow extreme heating of the side exposed to the Sun. And the relatively slow rate of rotation (once every 58.6 days) means that the night side can lose large quantities of heat by radiation.

NEWS AND VIEWS

Does Zodiacal Light Intensity Vary?

ZODIACAL light is the term used to describe the faint cones of light that extend away from the Sun in the ecliptic plane, or zodiac, of the sky. It is visible to the naked eye and can be best seen from a high mountain in the tropics where it appears in the western sky for an hour or so after the end of evening twilight, or in the east for a similar period before the beginning of dawn. The narrow cone of light stands up above the horizon and reaches about halfway to the zenith. It shares the apparent diurnal motion of the sky and during the night sinks below the western horizon until, two hours or so after its first appearance at the end of twilight, only the faint upper portions remain visible. The cone is widest at the base, where it is of comparable intensity to the Milky Way, and narrows and grows fainter towards its apex. Studies of the spectrum of this light indicate that it is caused by sunlight scattered from small, solid interplanetary dust particles. These dust particles pervade the entire Solar System and by scattering sunlight they produce about one-third of the total light shining on the Earth's surface on a moonless night (the remainder is due to airglow and background starlight). Again, using spectroscopic observations the Doppler shift of several of the Fraunhofer lines in the spectrum of the light can be measured. Radial velocities determined from these observations indicate that essentially all the dust particles are in direct orbits around the Sun.

It has been deduced from polarisation observations that the zodiacal light could be produced either by many very small particles (submicron) or by fewer larger particles having rough surfaces. The similarity between the spectra of zodiacal light and Sun light supports the latter hypothesis and it is now generally believed that most of the light comes from particles smaller than $10\ \mu\text{m}$ (masses less than $10^{-9}\ \text{g}$). Over a period of about 10,000 years these particles will be dragged into the Sun by the Poynting-Robertson effect, whereby the particles lose angular momentum due to the uniform re-radiation of adsorbed solar radiation. So if the dust cloud is in a steady-state condition there must be a continual source of small particles. The exact nature of this source is still in some doubt because the dust introduced must not only be of the right size but it must also be in the right place in the Solar System. A considerable fraction will come from the breakup of cometary nuclei as they pass close to the Sun and this process leads to the formation of streams of dust particles around the orbit of the comet. These dust streams then decay into the Solar System dust cloud. Asteroidal collisions could produce sufficient dust outside the Earth's orbit, which would slowly spiral into the Sun due to the Poynting-Robertson effect. Lunar ejecta produced by meteorite impact have also been suggested.

One way of deciding between these different possibilities is to investigate the temporal constancy of zodiacal light. Continual changes in the brightness as a function of, for example, the Earth's position around its orbit could indicate that the dust cloud was not equidense but was made up of a collection of individual toroidal particle

streams. Constant brightness could, on the other hand, indicate that asteroidal debris was the main component of the cloud and/or that the meteor streams only contain large particles (mass greater than $10^{-6}\ \text{g}$) which only over a period of about 10,000 years break up into smaller zodiacal dust particles and diffuse into the cloud. A third possibility is that new streams do contain many small particles but that these are perturbed from the stream orbit very quickly. It has also been suggested that the dust does not originate in either comets or asteroids but is just an extension of the outer solar corona and has a common physical origin. These last two suggestions would both give constant brightness.

Results of a satellite-borne experiment to measure the brightness of zodiacal light (6530 Å) as a function of ecliptic latitude and the position of the Earth around its orbit are set out on page 26 of this issue of *Nature*. The satellite used, D2A 'Tournesol', was in a low altitude orbit and reaching a maximum height of 700 km above the Earth's surface. Levasseur and Blamont of the Service d'Aéronomie du Centre National de la Recherche Scientifique obtain measurements of the zodiacal light intensity at 90° elongation, that is in the plane perpendicular to the Earth-Sun line, which agree very well on normal days (that is, for most solar longitudes) with previous measurements by other researchers. On certain days, however, the zodiacal light intensity increased by up to 100% above the normal value, and this increase lasted a few days. By making measurements in consecutive years Levasseur and Blamont found the variations in intensity to occur at the same positions around the Earth's orbit. They conclude that these increases were caused when the Earth passed through a meteor stream, the 100% increase on November 1971, which remained 50% above the normal level for six days around the maximum, being the result of an encounter with the Andromedid stream, a toroid of particles in space produced by the decay of comet Biela.

The April Lyrids have also been detected, and one very interesting fact emerging from the observations is that width of the stream of small dust particles detected by the zodiacal light observations appears to be twice as wide as the stream of much larger (mass $\sim 10^{-1}\ \text{g}$) particles observed as visual meteors. Levasseur and Blamont conclude that the cloud of zodiacal dust particles is not uniform but consists of a collection of streams of particles, created by the decay of recent comets; these streams have a relatively short lifetime and diffuse into a more general background on account of the Poynting-Robertson effect. Interparticle collisions and planetary perturbations can also cause this stream decay.

Interestingly, Alexander, Arthur, Bohn and Smith (*Space Res.*, **13**; 1973) have also detected increases of up to 100% in the density of picogram particles, in this case in selenocentric space, by using microphone sensors on board the satellites Lunar Explorer 35 and OGO III. These increases were found to coincide with the major meteor showers.

A slightly cautionary note, however, must be intro-

duced. Sparrow and Ney (*Science, N.Y.*, **181**, 438; 1973), who have been measuring the intensity of the zodiacal light for four years from the satellite OSO-5, have failed to detect any temporal variations in the brightness or polarisation and have concluded that this variation if present at all is less than $\pm 10\%$ of the mean value. Sparrow and Ney discount all the many previous observations which purport to show correlations between zodiacal light intensity and solar surface brightness, magnetic storms, lunar phases, the position of Comet Encke, the Earth's position around its orbit and the eleven-year solar activity cycle.

At present these contrasting observations make the choice of a hypothesis to explain the origin of the zodiacal dust cloud very difficult. D. W. H.

New Look at Chromatin

In the past, attempts to relate the structure of chromatin to its function have lacked incisiveness because it has not proved possible to test directly for the expression of a given gene. It can be argued, for example, that looking at the physical and chemical properties of chromatin or the rates of transcription *in vitro* from chromatin templates does not give conclusive results since they fail to establish a direct relationship between the observed phenomena and specific gene expression.

Because of this criticism some workers have tried to analyse the RNA transcribed *in vitro* from chromatin by hybridising it to homologous DNA in conditions of RNA excess. In this type of analysis increasing concentrations of RNA are hybridised to a fixed quantity of DNA until a saturation level is reached. From this figure the fraction of active DNA in chromatin was estimated and it was concluded that only certain of the DNA sequences in chromatin are transcribed. The same type of analysis has been used to compare the sequences of two RNA populations by comparative hybridisation. In some of these studies the RNAs transcribed from different chromatin templates were found to contain markedly different types of sequences (for example, Paul and Gilmour, *J. molec. Biol.*, **34**, 305; 1968). It was argued that the template activity of DNA in chromatin is restricted in such a way that only tissue specific sequences are transcribed and that this provides the basis for the observed differences.

As knowledge of the complexity of eukaryotic DNA developed it became apparent that such hybridisation studies only detect RNA sequences which are transcribed from the repetitive fraction of the DNA. Recent studies of Harrison *et al.* (*Nature*, **239**, 219; 1972) and Bishop *et al.* (*Nature*, **235**, 231; 1972; and *Nature new Biol.*, **241**, 204; 1973) have shown that a tissue specific mRNA, globin mRNA, is transcribed from the unique DNA fraction. If this is generally true for most other mRNAs, then RNA excess hybridisation studies will not reveal differences in messenger sequences. The fact that tissue specific differences were detected within the repetitive DNA fraction is therefore intriguing.

A new approach to the analysis of chromatin function is now available as a result of the recent demonstration that globin mRNA can serve as template for the RNA dependent DNA polymerase (reverse transcriptase) from avian myeloblastosis virus to give a complementary DNA

(cDNA) copy of globin mRNA. Several workers have devised kinetic analyses in which RNA populations can be tested for the presence of globin mRNA by hybridisation to cDNA. When applied to the RNA transcribed *in vitro* from chromatin this test provides a far more exact analysis.

At this year's Cold Spring Harbor Symposium two groups of workers reported studies in which RNA transcribed by *Escherichia coli* polymerase from haemopoietic chromatin was examined in this way. Gilmour and Paul of the Beatson Institute for Cancer Research, Glasgow, compared the RNAs transcribed from mouse foetal liver (a haemopoietic tissue) and mouse brain chromatin by hybridising the RNAs to cDNA complementary to mouse globin mRNA. The results show that RNA transcribed from foetal liver chromatin contains globin mRNA sequences (1–2 parts in 10^5), whereas RNA transcribed from brain chromatin contains no detectable sequences. Axel *et al.* at the National Institutes of Health, Bethesda (see *Proc. natn. Acad. Sci., U.S.A.*, **70**, 2029; 1973), made a similar comparison between RNAs transcribed from duck reticulocyte and duck liver chromatin and found that 7 parts in 10^5 of reticulocyte chromatin RNA corresponded to duck globin mRNA whereas liver RNA contained no globin sequences.

Both groups eliminated the possibility that the globin mRNA had arisen by contamination with cellular RNA rather than by *de novo* synthesis, by incubating the haemopoietic chromatin in the absence of polymerase and finding, after adding carrier RNA, no material hybridising to cDNA. Furthermore, Gilmour and Paul isolated the hybrid formed between cDNA and RNA transcribed from mouse foetal liver chromatin on CsCl gradients. By labelling the RNA with ^{32}P it was possible to estimate that most of the hybridisable RNA arose by polymerase action and not cellular contamination. These results demonstrate that the transcription of DNA in chromatin is restricted in a very specific way and that this property survives the chromatin isolation procedures. Moreover, the findings show that bacterial polymerase can transcribe the globin gene and that the sequences transcribed by it are subject to a control mechanism. The conclusions then are very similar to those obtained from the earlier experiments in which RNA excess hybridisation was used.

The finding that tissue specific differences exist in the RNA transcribed from reiterated DNA sequences may be of considerable importance. By annealing RNA transcribed from chromatin in conditions of DNA excess, Axel *et al.* demonstrated that most of the RNA is transcribed from unique DNA sequences and only a small part comes from repetitive DNA. A similar analysis of *in vivo* nuclear RNA by Melli *et al.* (*Nature*, **231**, 8; 1971) gives an analogous result. It is now becoming clear that there is a relationship between unique and repetitive sequences both in RNA and DNA. Firtel and Lodish (*J. molec. Biol.*, **79**, 295; 1973) examined the nuclear mRNA precursor of *Dictyostelium* and found that about 25% of the sequences are transcribed from repetitive DNA, the remainder being unique. Most of the repetitive sequence, which is at the 5' end of the RNA, is removed during nuclear processing; however, a small portion accompanies the RNA into the cytoplasm. Similarly, Dina *et al.* (*Nature new Biol.*, **242**, 101; 1973) found that mRNA from the polysomes of *Xenopus* embryos contain two types of sequence, one which hybridises to the repetitive DNA and the other which is complementary to unique

DNA. For *Xenopus*, Davidson *et al.* (*J. molec. Biol.*, **77**, 1; 1973) have presented evidence that the types of sequence are interspersed throughout the genome and they propose that 200–400 bases of unique sequence alternate with longer unique sequences of average length 600–900 nucleotides, large enough to accommodate a single gene.

It is attractive to speculate that the short repeated sequences represent control elements which regulate the transcription of adjacent unique sequences. As already noted some of these repeated sequences are transcribed and indeed tissue specificity in the repetitive sequences of *in vivo* RNA is demonstrable in the earlier experiments of Shearer and McCarthy (*Biochemistry*, **6**, 283; 1967). The possibility that there is a degree of specificity in the repetitive RNA sequences from different tissues provides an explanation of why RNA excess experiments with chromatin-primed RNAs show tissue specificity. Hence within the repetitive sequences there may be broad specificities which reflect in a general way the specific mRNA sequences of a given tissue. Obviously because of the relatedness of repetitive sequences and the present uncertainty about their function this is not a particularly definitive parameter of gene expression. Hybridisation to cDNA complementary for a known mRNA clearly offers the most exact method available.

At the Cold Spring Harbor Symposium, the Glasgow group also reported results which indicated how this new approach might be used to identify molecules concerned with the restriction of chromatin. It was found that when the structure of foetal liver chromatin is disrupted by dissociating the DNA and proteins in high salt-urea solutions and then the components reassociated by slowly dialysing away the salt, the resulting chromatin still serves as a template for globin mRNA sequences. This means that the specific way in which chromatin is assembled is an inherent property of the components themselves. Which are the molecules responsible for directing this self-assembly?

A preliminary investigation implicates molecules within the non-histone or acidic protein fraction of chromatin. Non-histone proteins from foetal liver were isolated free of DNA and histones on hydroxy-

apatite columns. This material was allowed to associate with mouse brain chromatin by the reconstitution process already described. It could be shown that globin mRNA sequences which are normally absent from brain chromatin transcripts are now detected in the RNA transcribed from brain chromatin reconstituted with liver non-histone proteins. This suggests that there is a component of liver non-histone which is responsible for controlling the expression of the globin gene.

The isolation and handling of non-histone proteins have now reached a stage where virtually pure fractions of individual components can be obtained. Although some of these are probably chromatin-associated enzymes or structural proteins rather than control elements, it is now possible for the first time to make this distinction and, hopefully by narrowing down the field, ultimately to identify the responsible molecules.

S. G.

MEDICAL RADIOLOGY

Benefits and Risks

from a Correspondent

PATIENTS undergoing medical radiology are subject to small, but not negligible, genetic and somatic hazards. If the risks and benefits could be quantified, a cost/benefit study could be undertaken and measures to reduce the detriment could be assessed realistically against the likely gain. This was the

main theme of a conference organised by the Society for Radiological Protection in Birmingham on October 9.

The evaluation of the risks involves four stages. First, the radiation doses to individual organs are determined by direct measurement or otherwise; next, for each organ the mean dose to the population is assessed, taking into account the number of patients involved, their age distribution and other factors; third, the biological effect of a given organ dose is estimated; finally, a monetary value is attached to a given detriment.

The radiation doses involved are known reasonably well. By far the largest contributor is diagnostic radiology and this field was reviewed by S. B. Osborn (King's College Hospital, London). The evidence is derived mainly from the 1960 and 1966 reports of the Adrian Committee. The mean genetically significant dose (GSD) from diagnostic X rays to the whole population of the United Kingdom is about 15 mrad yr⁻¹, and the annual mean bone marrow dose is about 32 mrad. In other countries the GSD ranges from 1 to 50 mrad depending on the amount of radiology undertaken and the techniques used. Osborn pointed out that very large variations occur from hospital to hospital and the United Kingdom detriment could be reduced considerably if all institutions reached the standard of the best: this could not, however, be achieved without additional expenditure.

The contribution of radiotherapy to the mean annual GSD is about 5 mrad, whereas that from radioisotope tests is currently about ten times lower. The use of unsealed radioisotopes, however,

Conditions for Restriction in *E. coli*

MANY strains of *Escherichia coli* recognise the DNA of other strains and of phage. Recognition is followed by hydrolysis of the invading DNA, with a strain-specific endonuclease, unless the DNA is modified (by glucosylation and methylation) or mutated—presumably at the recognition site (SB site). A DNA duplex with only one strand modified is protected from degradation. Some experiments by Hartman and Zinder, of the Rockefeller University of New York, suggested that in some FI phage crosses of DNA duplexes only one strand is mutated at an SB site. They wondered how this mutant hybrid would compare with a modified hybrid when challenged with restriction enzymes and so, together with their colleagues Vovis and Horiusha, designed experiments to tackle the problem. Next Wednesday's *Nature New Biology* (November 7) contains an account of this work.

DNA heteroduplexes were made

in vitro by annealing the wild-type DNA of phage FI with alkali denatured RFIII/PL (that is, full length, linear, double stranded DNA enzymatically prepared from the replicating form of the virus-RFI, with restriction enzyme PL). The resulting heteroduplex, RFII, is circular, double stranded with at least one single strand nick.

The phage FI has two sites SB₁ and SB₂ which confer susceptibility to *E. coli* B restriction. By making heteroduplexes in which one or other of the DNA strands was modified or mutated at the SB sites, and testing for restriction with *E. coli* enzyme B, it was possible to confirm that both modification and mutation of either strand of a DNA duplex at the SB site protect the molecule from restriction.

The authors were not able to determine whether SB mutant hybrids can be modified *in vivo* or *in vitro*, but they are at present working on this question.

is doubling every 3 yr. R. E. Ellis (University of Leeds) has found (ICRP Publication 17) that most individual radionuclide investigations give rise to somatic and genetic doses to patients comparable with those from X-ray examinations, but there are important exceptions and he proposed a set of maximum organ doses (for example, 5 rad for non-pregnant adults) for these tests.

The assessment of the biological effect of small radiation doses was discussed by J. Rotblat (St Bartholomew's Hospital Medical College, London). This is the most difficult step of all, since the effects must be extrapolated from the observed results of irradiation at relatively high dose levels. In the absence of direct evidence, a linear extrapolation is often assumed, but Rotblat thought that this may sometimes underestimate the effect. The evidence from Hiroshima indicates an annual death rate from radiation-induced cancer of all types of $\sim 6/10^6$ adults per rad. For young persons, however, the rate per rad seems to be several times higher, and it is still higher for embryos. For continuing exposure the induction rate depends on the latent period and the number of remaining years of life during which cancer may become manifest. Rotblat concluded that medical uses of radiation in the United Kingdom may lead to an annual cancer rate of 150–750, with perhaps a further 25–600 diseases or abnormalities of genetic origin.

G. Webb (National Radiological Protection Board) discussed the methodology and potential uses of a cost/benefit study in this field. Although a rigorous analysis is not yet feasible, useful results can still be obtained. The overall cost to society is reduced if patient doses are held at the lowest level consistent with a high rate of successful diagnosis and treatments. According to ICRP Report 22 the cost of the detriment associated with 1 man-rad is £10–£100. If the mean GSD to the UK population is 20 mrad, the annual cost of the genetic detriment alone is $\text{£}10^7\text{--}10^8$, a significant fraction of the total cost of the National Health Service ($\sim \text{£}2 \times 10^9$ yr⁻¹). Webb concluded that the British people can afford to invest a little more each year in the health of future generations.

PHARMACEUTICS

Safety of Contraceptives

from a Correspondent

A MEETING organised by the World Health Organisation was held in Geneva from September 16 to 20 to discuss the use of pharmacological models in the assessment of toxicity and side effects of

fertility regulating agents. The meeting reflected the uncertainty felt by many involved both in the development of new fertility regulating agents and the continued use of presently available ones concerning the assessment and monitoring of toxicity and side effects. A major part of the deliberations was concerned with the extent to which studies performed on animals could be extrapolated to man. The usefulness of the various tests of toxicity and anti-fertility carried out in a number of species was reviewed. To have predictive value these tests should be performed in species in which the reproductive mechanisms, toxic reactions and metabolic disposition of the agents are similar to those in humans. Because of the wide variability of these parameters in different species a number of different species would probably have to be used, an obviously unsatisfactory solution.

If animal models are unsuitable for assessing toxicity, the careful monitoring of subjects using the regulatory agents is of extreme importance and this again raises special problems. These agents are used by normal healthy women over long periods of time and often with little medical supervision. Side effects which occur with a high frequency would be quickly noted but those which occur with a low frequency would be much more difficult to detect. It is these low frequency side effects which are difficult, if not impossible, to detect in animals. As expected, the question of carcinogenicity of presently used hormonal contraceptives provoked much discussion, although those who suggest on theoretical grounds that the oral contraceptives might be carcinogenic in humans have difficulty in finding evidence to support their views. No satisfactory model is presently available to test for carcinogenicity. In considering contraceptive drugs the return of fertility at the end of the treatment period has to be ascertained. The possibility that women might become pregnant while taking, or shortly after having taken, the drug necessitates screening for teratogenic and mutagenic effects.

The requirements for toxicity testing of anti-fertility agents were discussed by representatives of the national drug regulatory agencies with particular consideration to the possibility of standardising many of the requirements on an international basis. These requirements must change in the light of new knowledge. The advantages and disadvantages of methods available for monitoring side effects in humans were also reviewed. The evaluation of reported side effects is complicated by the incidence of placebo reactions and these have not been taken into account in many trials. In addition, variations in response of women of different ethnic

origins to the same contraceptive drug are important. The special requirements for toxicity testing of long acting and of post-coital contraceptives, of spermicides, of various types of intrauterine devices and of the prostaglandins, all of which pose special problems, were also discussed.

It would not be advantageous to increase the amount of animal toxicity testing since this would increase the cost of research and development and, in the opinion of one speaker, "lead to a decreased interest on the part of the pharmaceutical industry to develop new agents. If this were to happen it may ultimately be more disastrous for the survival of large parts of the world population than the limited risk of even serious adverse effects of oral contraceptive preparations". It is hoped that advances in contraceptive technology would lead to a decrease in the amount of toxicity testing that needs to be carried out and hopefully shorten the time between animal testing and preliminary evaluation in humans.

Not unexpectedly, at the end one felt many questions remained unanswered, more research needed to be done, present methodology required improvement and many more discussions were imperative.

CELL BIOLOGY

Control of Proliferation

from a Correspondent

THE sixth meeting of the European Study Group for Cell Proliferation, which was held in Moscow from September 25 to 28 at the Institute of Molecular Biology of the Academy of Sciences of the USSR, took the general title "Molecular Mechanisms and the Control of Cell Proliferation".

Among the invited participants Professor J. M. Mitchison (University of Edinburgh) reviewed the concept of cell cycle markers, within which he included any detectable event which is associated with a localised region of the intermitotic period. Markers fall into three categories: morphological events such as mitosis or abrupt changes in the structure of the cell surface; biochemical events such as the initiation of DNA synthesis or the induction of specific enzymes; transition points at which metabolic inhibitors either begin or cease to be effective. The markers that are available within any one proliferating cell system indicate detectable points in the sequence of gene expression through the cell cycle. In some cases the blocking of one event in this sequence may suppress later events. Other examples can be found in which the sequence of events that make up the "DNA synthesis-division" cycle may to some extent be dissociated

from the sequence of the "cell growth" cycle.

At present a great deal of interest centres on the ability of proliferating cells to move into a state in which the DNA synthesis-division sequence is interrupted, as well as on their ability to respond to a suitable stimulus by continued proliferation. Yu. M. Vasiliev (Institute of Oncology, Moscow) reviewed the evidence for this in cultures of normal and neoplastic cells, which can enter a quiescent state either as a result of medium deprivation or confluency and renew proliferation following mechanical damage, the addition of fresh serum or treatment with a variety of chemical agents.

An important contribution to understanding of the nature of contact inhibition of growth came through the work of A. Zetterberg (Karolinska Institute, Stockholm) who has studied the approach to confluency in cultures of mouse kidney epithelial cells. When the cells were grown at low cell densities on a solid support, a thin web of cytoplasm formed around them, clearly demonstrable in the interference microscope, to which the term 'lamellar cytoplasm' was given. Detailed studies of the relationship between cell surface area and thymidine-labelling index led to the hypothesis that the cellular proliferation rate is largely determined by the area of the lamellar cytoplasm, with some dependence also on the nutrient quality of the medium. The biochemical changes that take place in confluent cell monolayers following stimulation by a change of medium were described by R. Baserga (Temple Medical School, Philadelphia). In cultures of normal human fibroblasts, an increase in the synthesis of non-histone chromosomal protein is detectable within 30 min of stimulation, closely followed by an increase in chromatin template activity, but neither of these early responses was found following stimulation of virus-transformed fibroblasts. The proffered papers, of which there were more than fifty, illustrated the existing wide interest in the control of cell proliferation both *in vivo* and *in vitro*, with sessions devoted to cell proliferation in haemopoietic tissues and to the possible role of chaperones in tissue homeostasis.

The European Study Group for Cell Proliferation, which was formed in 1967 under the auspices of the Coordinating Committee for Human Tumour Investigations, has now gained affiliation to the European Cell Biology Organisation. Its meetings have been designed to span a wide range of interests from the biochemistry of cell proliferation, through the study of cell and tissue kinetics, to the attempt to relate cell proliferation to therapeutic response in cancer. The next meeting will be in Amsterdam in the spring of 1975.

CELL BIOLOGY

Proteases and Growth

from a Correspondent

THE intriguing correlation between proteolytic activity, high agglutinability in the presence of plant lectins, and cell growth has been studied extensively in recent years. Transformed cells are readily agglutinable by lectins and continue to grow in conditions which arrest normal cells. Normal cells are much less readily agglutinated but on treatment with proteases they become agglutinable and, it is claimed, start growing again. It has been proposed, on the basis of these observations and others, that proteases produced by transformed cells act upon the surfaces of the cells and trigger them into growth.

This simple picture has now been questioned by Glynn, Thrash and Cunningham who report (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 2676; 1973) that pronase treatment of 3T3 cells which have stopped growing renders the cells agglutinable by lectins but does not start them growing again. The increase in agglutinability, whatever it means, is in agreement with results from a number of laboratories, notably that of Burger (see *Fed. Proc.*, **32**, 91; 1973, for review) and Sachs, but the failure to stimulate

growth suggests that the alteration in cell surface produced by pronase and detected by lectins is not sufficient to trigger growth as has been suggested. Earlier reports have claimed that proteases, including pronase, when applied to cells, including 3T3, do start them growing (Burger, *Nature*, **227**, 170; 1970; Sefton and Rubin, *Nature*, **227**, 843; 1970).

There seems to be a direct conflict of results here. One might argue that Glynn *et al.* had damaged their cells so that they could no longer respond to growth stimuli. They show, however, that serum added after the pronase treatment is still effective in growth stimulation, although the response was not quite so marked as when the pronase treatment was omitted. They also state that the treated cells still respond to cortisol, another growth initiator.

The solution to this conflict could be in minor differences in procedure: perhaps the media of Burger and of Sefton and Rubin were less completely depleted of serum factors than those of Glynn *et al.* thus allowing or assisting the cells to respond to a growth stimulus by the pronase. The answer will have to await further experiments but it is clear from the results of Glynn *et al.* that one can separate the surface changes produced by proteases from any growth stimula-

Vesicular Stomatitis Virus Cores add Poly(A)

VESICULAR stomatitis virus (VSV) is a bullet shaped, negative strand virus that infects a wide variety of animal cells. Its genome is a single large piece of RNA that acts as a template for a virion-associated polymerase. This enzyme can be unmasked *in vitro* by non-ionic detergents such as NP 40. The RNA made by detergent-treated virions is considerably smaller than the genome, and complementary to it, but similar RNA species are found to be associated with the polysomes of VSV infected cells.

The MIT group of Baltimore, Lodish and colleagues have recently shown that these RNA molecules code for authentic VSV proteins in the wheat-germ cell-free protein synthesising system, so it seems legitimate to call them mRNA. Mudd and Summers (*Virology*, **42**, 958; 1970) showed three years ago that these messages contain poly(A), but a certain confusion has arisen as to when, where and how the poly(A) gets added.

Everybody agrees that the genome lacks the poly(U) tracts which would be necessary to code for the poly(A), but Roy *et al.* (*J. Virol.*, **11**, 915; 1973) recently said that the detergent-disrupted virions fail to make any poly(A). At the same time, Galet and Prevec (*Nature new Biol.*, **243**, 200; 1973) found that cytoplasmic extracts of VSV

infected cells would make mRNA which had the poly(A) stretches. These results seem to suggest that the host cell has a cytoplasmic enzyme which can add poly(A) to a viral RNA primer. This hypothesis is probably unnecessary, however, for Villareal and Holland report some experiments with detergent-treated VSV in *Nature New Biology* next Wednesday (November 7). They found that if they purified the cores by gel-filtration on Biogel A-5M they (1) obtained considerably higher activity and (2) the mRNA produced contained poly(A).

Unlike the activity found in Vaccinia virus cores (Kates and Beeson, *J. molec. Biol.*, **50**, 19; 1970), VSV cores need all four nucleoside triphosphates to make poly(A), suggesting that a primer is required to which the poly(A) is added. The nature of the primer is unclear, however, for Villareal and Holland find that even the small pieces of RNA produced by the defective interfering 'T particles' of VSV can have normal poly(A) added to them. Nor is it clear whether the primed but template-independent addition of poly(A) is made by the RNA-dependent RNA polymerase, or whether some other component of the purified cores—perhaps the so-called NS protein—is responsible.

tion. So, if proteolytic digestion assists in removing controls involved in density dependent inhibition of growth, which is not ruled out by these results, it does not manage it by itself. This conclusion is perhaps not surprising but worth stating in any case, especially for those cell biologists who are studying the role of serum factors and hormones in growth control.

THEORETICAL CHEMISTRY

Quantum Chemical Game

from our Molecular Physics Correspondent

ALL too often the complexities of the many-electron problem in chemistry lead to a frontal, and sometimes premature, assault by computer, relieved only occasionally by the elegance of a result from group theory or elsewhere. So familiar has this pattern become that it is a pleasant surprise to be presented with a simplification that is both unusual and elegant and, in its way, outright amusing.

Such a description may justly be applied to the paper entitled "A Game Theoretic Model for the Determination of Charge and Configuration in Metal Complex Compounds" by Haberditzl and Bartel (*Chem. Phys. Lett.*, **19**, 432; 1973). The authors show how at least one stage of the, in principle enormously complicated, problem of calculating the distribution of electrons between the central ion of a metal complex and its neighbours can be reduced to a simple exercise in the theory of games, the ion and its neighbours 'competing', as it were, for the electrons available. The type of idealised game involved proves to be quite a simple version of the 'two-person zero-sum' game in which two players seek an optimal course of action to maximise their chance of gain from a fixed premium. The various 'pure strategies' in the game correspond to suitable wave functions for the ion and the ligand system, and the 'payoff matrix' gives the hypothetical gain of electrons by the central ion for differing combinations, with due allowance for symmetry.

Of course the elements in the latter must be calculated by whatever means are to hand—inevitably some form of perturbation theory—and it is here that the full difficulty and scope for ingenuity in the problem very much remain. Yet, once the 'payoff' conditions have been specified, the optimal strategy for the central ion can be computed in a very simple manner and, moreover, in a single step (with considerable advantage over the laborious and somewhat fickle iterative methods used up to now).

Specialists will no doubt be quick to delimit the scope and practicality of the method, but it seems entirely possible that it will find applications to 'competi-

JUPITER

Plea for Observations

by our Cosmology Correspondent

PIONEER 10 is now rapidly approaching Jupiter, and in a recent issue of *Icarus* (**20**, 52; 1973) Coffeen, of the University of Arizona, puts in a plea for ground based observations to coincide with those of the probe. The period of particular interest is from November 28 to December 10, and there is a need for ground based photography, spectroscopy, photometry and polarimetry; during that period, Jupiter will be at a declination of $18^{\circ}.8$, with phase angle 9° , 4.1 h east of the Sun, so that southern latitude observations at around the time of evening twilight will be most effective.

tive' situations other than that between a metal ion and a ligand system. At the same time no one should go out of their way (as the authors conspicuously refrain from doing) to see anthropomorphic subtleties in the interatomic battle for electrons. The game-theory insight reveals a curious and perhaps far reaching new minimum principle, separates a messy calculation into two usefully distinct stages, and provides an illuminating mapping of one computational problem into a better known one. Quantum chemistry, perhaps of all theoretical sciences one of the most liable to be seen as a confusion of woods and trees, can certainly do with more adventurous touches of this kind.

PETROLOGY

Kimberlite Conference

from a Correspondent

ALTHOUGH kimberlites provide a more thorough sampling of the upper mantle than any other type of magmatic rock, they have never before formed the focal point of a major international conference. This was largely redressed when the first international conference on kimberlites was held, appropriately in South Africa, at the University of Cape Town from September 23–29.

In the session on kimberlite geology, descriptions were given of less well-known kimberlite provinces in North America, Greenland and South Africa, and M. Bardet (Bureau de Recherches Géologiques et Minières, Orléans) described kimberlites from West Africa that lack the normal kimberlite 'indicator' minerals (pyrope, picroilmenite) and suggested that many of these atypical kimberlites are yet to be discovered, having been missed by current prospect-

ing techniques. Although there was general agreement on an explosive origin of kimberlite diatremes, there was considerable debate as to whether the explosion mechanism results from high pressure gases within the kimberlite magma or is due to super-heating of groundwater by the ascending magma. In this context, the D/H and $^{18}\text{O}/^{16}\text{O}$ studies by S. M. F. Sheppard (Scottish Universities Research Reactor Centre, East Kilbride) indicated the involvement of warm groundwater in the formation of some diatreme kimberlites. Micro-probe analyses of the hitherto neglected groundmass minerals in the kimberlite matrix have now provided valuable information on the physical conditions prevailing during the crystallisation of the kimberlite matrix. This was exemplified by S. E. Haggerty (University of Massachusetts) whose work on the opaque phases has revealed considerable variation in the redox conditions, cooling rate and solid-solid, solid-gas and solid-liquid reactions during crystallisation. Haggerty also reported the occurrence in kimberlite of a new barium-vanadium titanate, and the first terrestrial occurrence of armalcolite.

In the sessions on xenoliths, two aspects made the most impact. Until now virtually no work has been carried out on the petrofabrics of kimberlite xenoliths, but A. Nicolas (University of Nantes) and B. Harte (University of Edinburgh) both reported a wide variety of deformation and recrystallisation features that have been imposed on these rocks within the upper mantle. The second aspect linked up strongly with the deformation studies of Nicolas. F. R. Boyd (Geophysical Laboratory, Washington) and P. H. Nixon (Department of Mines, Lesotho) showed that highly-sheared lherzolites have equilibrated at relatively high temperatures ($1,300\text{--}1,400^{\circ}\text{C}$) compared with the more normal granular lherzolites ($950\text{--}1,100^{\circ}\text{C}$), and together with the granular lherzolites could be used to infer a Cretaceous geothermal gradient; also Boyd and Nixon interpreted the shearing as due to the movement of the African Plate during the breakup of Gondwanaland.

The geochemistry of sheared lherzolites provided another focus of attention. They contain more CaO and Al_2O_3 than the granular lherzolites (and hence more potential basalt) but A. J. Erlank (University of Cape Town) showed them to be strongly depleted in both Nb and Zr. In addition N. Shimizu (Geophysical Laboratory, Washington) reported that the clinopyroxenes in the sheared lherzolites have very high K/Rb ratios ($2,000\text{--}2,200$), extremely high K/Cs ratios ($1,000,000\text{--}3,000,000$), and low $^{87}\text{Sr}/^{86}\text{Sr}$ ratios ($0.7027\text{--}0.7038$). This apparent clash between the major and trace element evidence, together with the wide-

spread occurrence of sheared lherzolites, underlines the need for more data on this important rock type.

The inclusions in diamonds have already provided valuable information on the phases coexisting with diamonds. With the increased sophistication of chemical techniques even more data have been provided by these unique sources of upper mantle information. For example, H. Allsopp (Bernard Price Institute, University of the Witwatersrand) reported U/Pb ages for diamonds from the Premier Mine, and H. Fesq (NPRU, University of the Witwatersrand) was able to show, on the basis of analysis of tiny drop-like inclusions within diamonds, that the liquid from which diamond crystallises is rich not only in siderophile elements but also in carbonate and sulphur.

The genesis of kimberlite was the subject of several papers on experimental petrology. There were two opposing viewpoints: (1) that kimberlite results from fractionation of a picritic parent, and (2) that kimberlite is an incipient melt from a phlogopite-bearing parental lherzolite. In the context of the second viewpoint, several authors reported that, although in the system peridotite-H₂O the initial melt is silica-saturated, when CO₂ is the dominant vapour phase the initial melt is silica-undersaturated. In a wider context, there seemed to be general agreement among delegates that there is a genetic link between kimberlite and carbonatite.

SUPERCONDUCTIVITY

Stimulated Tunnelling

from our Condensed Matter Correspondent Granqvist and Claeson of the Chalmers University of Technology in Gothenburg report in a recent issue of *Physical Review Letters* (31, 456; 1973) that they have observed some interesting new structure in the current-voltage characteristics of superconducting tunnel junctions which may, they suggest, be attributable to the stimulated emission of phonons.

Tunnelling is a phenomenon which occurs when two conductors are separated by a very thin non-conducting barrier: according to quantum mechanics there is a finite probability that an electron approaching the barrier from one side may spontaneously appear on the other side. If a small voltage is applied across the junction, a current will flow from conductor A which is at the higher potential, because it will have a large number of electrons which can tunnel across into empty states of the same energy in conductor B, on the other side of the barrier. A current does not flow in the reverse direction because there are no empty states in A of the same energy as that

of even the highest states in B. Nature permits only one electron per quantum state so that, if no empty states of appropriate energy are available, tunnelling cannot occur.

In the case of a superconductor, there is an energy gap 2Δ separating the superconducting, paired, electron states from the normal single electron states above them. For temperatures well below that of the superconducting transition, all the superconducting states will be occupied and all the normal ones empty. Tunnelling between two superconductors cannot occur, therefore, until the applied voltage V is sufficient to raise the potential of A to the extent that some of its occupied states reach the same energy as some of the empty states above the energy gap in B, which clearly requires $eV = 2\Delta$. The characteristic of such a junction is therefore: zero electron tunnelling current i up to the so-called gap voltage $2\Delta/e$; a very rapid increase in i as V just exceeds $2\Delta/e$, because of the particularly large density of permitted quantum states on either side of the energy gap; and a slower increase in i at larger values of V as tunnelling

takes place between states far from the energy gap whose density is much the same as that when the metal is in its normal state. The structure observed by Granqvist and Claeson consists of a series of unexpected wiggles in this latter part of the characteristic, and was only seen when electrode B was made exceedingly thin, about 1 nm.

The junctions were prepared by vacuum evaporation onto a germanium coated quartz substrate, using an elaborate technique in which the final, very thin, metal film electrode was deposited *in situ* in the cryostat at 0.3 K. The inner film was always of aluminium, which could be surface oxidised to produce the necessary layer of insulator, but a number of different superconductors were chosen for use as the thin outer electrode. The equipment was designed to measure, not i , but di/dV as a function of V , so the structure was resolved as sharp peaks. These peaks were invariably found to occur at potentials which were $2\Delta_i/e$ and $4\Delta_i/e$ above that of the main peak at $(\Delta_{Al} + \Delta_i)/e$, where $2\Delta_i$ is the energy gap appropriate to the very thin outer

Cavities in the Pulsar Magnetosphere

TAKE a highly magnetised sphere called a neutron star, and rotate it rapidly. Describe the region of space surrounding it. That, in essence, is the problem of the pulsar magnetosphere.

This is a very difficult problem, as it turns out, and indeed the complexity and variability of pulsar radiation lead one to expect that an apparently very simple problem may not have a simple, static, solution. Goldreich and Julian showed that the large electric fields induced by the rotating magnetic fields would be compensated for by a dense, charged magnetosphere, co-rotating with the star out to a 'velocity of light cylinder', where the co-rotation velocity approaches the velocity of light. Their solution was for a rotation axis coincident with a dipole magnetic axis. The perpendicular case is less tractable, but is known to have many similarities. The part of the problem which has so far received most attention is the configuration of the magnetic field lines as they cross the velocity of light cylinder. A new idea by Holloway (in *Nature Physical Science* next Monday, November 5) opens up the possibility of different configurations of charge inside the magnetosphere, and also gives a possible lead into the problem of the 'drifting sub-pulses'.

Holloway shows that a cavity within a positively charged portion of the magnetosphere would be stable, in the sense that the electric field at the boundary of the cavity would prevent

positive charges re-entering it. (There are no negative charges present, since there is complete charge separation in the magnetosphere.) The cavity could be a large sheet, dividing the magnetosphere into two regions. The situation is not necessarily static, however, since it is now possible for such a cavity to divide regions with different rotation speeds. In particular, there is likely to be a region which rotates faster than the star. This is interesting, because it provides a possible location for the emission of discrete sub-pulses of radio waves. These are often observed to 'drift', occurring earlier during each main pulse; the source thus super-rotates.

Differential rotation of this type would disturb the static picture, and the cavity would tend to fill through a viscous drift of particles. But there is a powerful dynamo in action around the star, and powerful centrifugal forces near the velocity of light cylinder. There is plenty of driving power available for re-creating the cavity. Holloway suggests that the centrifugal forces are responsible for depleting the charges in the cavity, but there is no detailed analysis as yet.

There is more to the problem of the rotating sphere than appears at first sight. It will not be sufficient to obtain a static self-consistent solution of the rotating charged magnetosphere. Holloway now explains that it may contain differential rotation; cavities, viscous drift and a centrifugal wind.

electrode and Δ_{Al} that for aluminium. This behaviour was consistently followed for outer electrode materials ranging from tantalum with $2\Delta_t = 1$ meV to lead with $2\Delta_t = 2.6$ meV, and in each case the structure diminished and finally disappeared as the outer electrode was made thicker.

Granqvist and Claesson suggest that these phenomena arise from the stimulated emission of phonons (quanta of lattice vibrational energy) in the outer electrode. The tunnelling electrons must arrive there with an energy $eV - \Delta_{Al} - \Delta_t$ above the top of its energy gap, and it is known that most of these first relax to states just above the gap through emission of so-called relaxation phonons of energy $eV - \Delta_{Al} - \Delta_t$, subsequently falling into paired superconducting states below the gap with emission of recombination phonons with energy $2\Delta_t$. If V is such that the recombination and relaxation phonons have the same energy, then there is a probability that the relaxation process will be stimulated by the $2\Delta_t$ phonons to occur faster than it otherwise would, so that, because a larger number of empty states will therefore be available into which tunnelling can occur, the current will seem to be anomalously large for that particular value of V , leading to a peak in di/dV . The required value of V is clearly $(\Delta_{Al} + 3\Delta_t)/e$, so one would expect a peak in di/dV , due to this effect, at $2\Delta_t/e$ above the gap voltage of $(\Delta_{Al} + \Delta_t)/e$, in agreement with experiment. Processes involving stimulated emission by two or more $2\Delta_t$ phonons should, by a similar argument, lead to further peaks at $4\Delta_t/e$, $6\Delta_t/e$ and so on, which is again consistent with experiment, although peaks beyond the one at $4\Delta_t/e$ are apparently too small to be observed.

The authors believe that these effects have not been observed previously because other workers were unable to prepare such thin outer electrodes: the thinner the electrode, the greater the density of recombination phonons, and so the larger becomes the probability of stimulated emission.

The density of these phonons must also be directly related to the recombination rate, so one would expect the magnitude of the new structure to depend markedly on the magnitude of the tunnelling current. A simple test of the theory would therefore be to repeat the experiment with junctions of different impedance, which can easily be arranged by varying the thickness of the oxide layer. The failure of a preliminary experiment of this nature to yield the anticipated result leads one to suspect that a complete explanation of Granqvist and Claesson's structure may turn out to be somewhat more complicated than they have suggested.

NUCLEAR PHYSICS

Resonance Transfer

from our Nuclear Structure Correspondent

WHEN an ion collides with an atom, the probability of electron transfer depends on the time they spend near each other (the collision time) and on the transfer time itself. If these times are similar, the transfer of one electron is most likely. If the collision time is twice the transfer time the electron can be transferred from the atom to the ion and back again, and so on. Since the collision time is inversely proportional to the relative velocity of the two atoms, the probability that an electron will be transferred from the atom to the ion attains peak values at a series of energies corresponding to one, three, five... transfers of the electron. A simple analysis shows that the cross section is of the form

$$\sigma(E) = A(E) + B(E)\cos^2(bE^{-1/2})$$

where $A(E)$ and $B(E)$ depend on the incident energy E and b is a constant. Measurements of electron transfer have been made by Ziembra and Eyerhart (*Phys. Rev. Lett.*, **2**, 299; 1959) that confirm this formula with surprising accuracy.

The simple theory works very well for the transfer of electrons between atoms because the electron is very light compared with the atoms themselves. If the transferred particle is comparable in mass to the colliding particles much of the simplicity is lost because of the increasing importance of recoil effects.

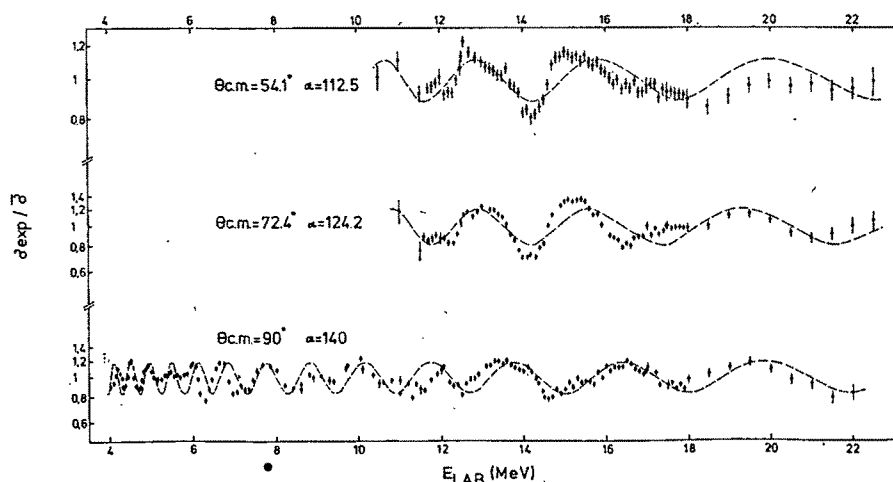
Resonant transfer processes, as they are called, have been looked for in nuclear reactions, and in particular it has been conjectured that they might be observable in neutron-proton collisions as multiple pion exchange or in heavy ion reactions as nucleon or cluster

exchange. Some indications of the characteristic signature of resonant transfer, a cross section following the formulae outlined here, have been found from time to time, but have not been substantiated by further work.

Recently a more convincing example of resonant transfer has been found in a study by Kelleter, Hrehuss and Mayer-Böricke (*Nucl. Phys.*, **A210**, 502; 1973) of the scattering of alpha particles by ${}^7\text{Li}$. The cross section of this reaction shows a rather irregular dependence on energy, as might be expected for such nuclei, but if it is plotted relative to the energy-averaged cross section an oscillatory behaviour is apparent, as shown in the figure. In particular, it shows an increase of 'wavelength' with energy very similar to that given by the resonant transfer, with small deviations readily attributable to the neglect of recoil and other effects in the simple theory. Since ${}^7\text{Li}$ can be considered as formed by a triton bound to an α particle, this oscillatory component of the reaction may be interpreted as due to transfer of a triton between the incident α -particle and the α particle in ${}^7\text{Li}$.

This interpretation is strengthened by an estimate of the parameter b , which is approximately given by $E_{\text{ex}}t_{\text{int}}/\hbar$, where E_{ex} is the average exchange energy and t_{int} the interaction time. The values of b obtained in this way are in qualitative agreement with those found by fitting the resonant transfer formula to the measured cross sections.

Further work needs to be done to develop a detailed theory of the process, taking into account the recoil effects and the presence of other reaction channels, and it would be useful if additional examples could be found experimentally. It is likely that such studies of resonant transfer reactions will provide a useful opportunity to develop nuclear reaction theory.



Ratio of the cross section for the elastic scattering of alpha particles by ${}^7\text{Li}$ to the energy-averaged cross section as a function of energy showing oscillatory structure interpreted as due to a resonant transfer of a triton between the two α particles. The dashed curves show the variation expected from the simple theory of the resonant transfer process.

The Logic of Animal Conflict

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Conflicts between animals of the same species usually are of "limited war" type, not causing serious injury. This is often explained as due to group or species selection for behaviour benefiting the species rather than individuals. Game theory and computer simulation analyses show, however, that a "limited war" strategy benefits individual animals as well as the species.

IN a typical combat between two male animals of the same species, the winner gains mates, dominance rights, desirable territory, or other advantages that will tend toward transmitting its genes to future generations at higher frequencies than the loser's genes. Consequently, one might expect that natural selection would develop maximally effective weapons and fighting styles for a "total war" strategy of battles between males to the death. But instead, intraspecific conflicts are usually of a "limited war" type, involving inefficient weapons or ritualized tactics that seldom cause serious injury to either contestant. For example, in many snake species the males fight each other by wrestling without using their fangs^{1,2}. In mule deer (*Odocoileus hemionus*) the bucks fight furiously but harmlessly by crashing or pushing antlers against antlers, while they refrain from attacking when an opponent turns away, exposing the unprotected side of its body³. And in the Arabian oryx (*Oryx leucoryx*) the extremely long, backward pointing horns are so inefficient for combat that in order for two males to fight they are forced to kneel down with their heads between their knees to direct their horns forward⁴. (For additional examples, see Collins⁵, Darwin⁶, Hingston⁶, Huxley *et al.*⁷, Lorenz⁸ and Wynne-Edwards⁹.)

How can one explain such oddities as snakes that wrestle with each other, deer that refuse to strike "foul blows", and antelope that kneel down to fight?

The accepted explanation for the conventional nature of contests is that if no conventional methods existed, many individuals would be injured, and this would militate against the survival of the species (see, for example, Huxley⁷). The difficulty with this type of explanation is that it appears to assume the operation of "group selection". Although one cannot rule out group selection as an agent producing adaptations, it is only likely to be effective in rather special circumstances¹⁰⁻¹². Consequently it seems to us that group selection cannot by itself account for the complex anatomical and behavioural adaptations for limited conflict found in so many species, but there must also be individual selection for these, which means that a "limited war" strategy must be differentially advantageous for individuals.

We consider simple formal models of conflict situations,

and ask what strategy will be favoured under individual selection. We first consider conflict in species possessing offensive weapons capable of inflicting serious injury on other members of the species. Then we consider conflict in species where serious injury is impossible, so that victory goes to the contestant who fights longest. For each model, we seek a strategy that will be stable under natural selection; that is, we seek an "evolutionarily stable strategy" or ESS. The concept of an ESS is fundamental to our argument; it has been derived in part from the theory of games, and in part from the work of MacArthur¹³ and of Hamilton¹⁴ on the evolution of the sex ratio. Roughly, an ESS is a strategy such that, if most of the members of a population adopt it, there is no "mutant" strategy that would give higher reproductive fitness.

A Computer Model

A main reason for using computer simulation was to test whether it is possible even in theory for individual selection to account for "limited war" behaviour.

We consider a species that possesses offensive weapons capable of inflicting serious injuries. We assume that there are two categories of conflict tactics: "conventional" tactics, *C*, which are unlikely to cause serious injury, and "dangerous" tactics, *D*, which are likely to injure the opponent seriously if they are employed for long. (Thus in the snake example, wrestling involves *C* tactics and use of fangs would be *D* tactics. In many species, *C* tactics are limited to threat displays at a distance, without any physical fighting. We consider a conflict between two individuals to consist of a series of alternate "moves". At each move, a contestant can employ *C* or *D* tactics, or retreat, *R*. If a contestant employs *D* tactics, there is a fixed probability that his opponent will be seriously injured: a contestant who is seriously injured always retreats. If a contestant retreats, the contest is at an end and his opponent is the winner. A possible conflict between contestants *A* and *B* can be represented in this way:

A's move C C C C C C C C C C C C C C C C C C C C C D

B's move C C C C C C C C C C C C C C C C C C C C C R

If a contestant plays *D* on the first move of a contest, or plays *D* in response to *C* by his opponent, this is called a "probe" or a "provocation". A probe made after the opening move is said to "escalate" a contest from *C* to *D* level. A contestant who plays *D* in reply to a probe is said to "retaliate". In the example shown above, *A* probes on his twelfth and twentieth moves; *B* retaliates after the first probe, but retreats after the second, leaving *A* the winner. At the end of a contest there are "pay-offs" to each contestant. The pay-offs are taken as measures of the contribution the contest has made to the reproductive success of the individual. They take account of three factors: the advantages of winning as compared with losing, the disadvantage of being seriously injured, and the disadvantage of wasting time and energy in the contest.

A "strategy" for a contestant is a set of rules which ascribe probabilities to the *C*, *D*, and *R* plays, as functions of what has previously happened in the course of the current contest. (No memory of what has happened in previous contests with the same or other opponents is assumed.) For computer simulation we programmed five possible strategies, each of which might be thought on *a priori* grounds to be optimal in certain circumstances. The strategies considered were as follows:

(1) "Mouse". Never plays *D*. If receives *D*, retreats at once before there is any possibility of receiving a serious injury. Otherwise plays *C* until the contest has lasted a preassigned number of moves.

(2) "Hawk". Always plays *D*. Continues the contest until he is seriously injured or his opponent retreats.

(3) "Bully". Plays *D* if making the first move. Plays *D* in response to *C*. Plays *C* in response to *D*. Retreats if opponent plays *D* a second time.

(4) "Retaliator". Plays *C* if making the first move. If opponent plays *C*, plays *C* (but plays *R* if contest has lasted a preassigned number of moves). If opponent plays *D*, with a high probability retaliates by playing *D*.

(5) "Prober-Retaliator". If making the first move, or after opponent has played *C*, with high probability plays *C* and with low probability plays *D* (but plays *R* if contest has lasted a preassigned number of moves). After giving a probe, reverts to *C* if opponent retaliates, but "takes advantage" by continuing to play *D* if opponent plays *C*. After receiving a probe, with high probability plays *D*.

The contestants were programmed as having identical fighting prowess, so that they differed only in the strategies they followed. The five strategies represent extremes, but from results with these it is possible to estimate the results likely to be found with intermediate types. The Hawk strategy is a "total war" strategy; Mouse, Retaliator, and Prober-Retaliator are "limited war" strategies. The question of main interest is whether individual selection will favour the former or one of the latter types.

The Simulation Test

The five strategies determine fifteen types of two-opponent contests. Two thousand contests of each type were simulated by computer, using pseudo-random numbers generated by an algorithm to vary the contests. The following probabilities were used: Probability of serious injury from a single *D* play=0.10. Probability that a Prober-Retaliator will probe on the opening move or after opponent has played *C*=0.05. Probability that Retaliator or Prober-Retaliator will retaliate against a probe (if not injured) by opponent=1.0. Pay-offs were calculated as follows: Pay-off for winning=+60. Pay-off for receiving serious injury=-100. Pay-off for each *D* received that does not cause serious injury (a "scratch")=-2. Pay-off for saving time and energy (awarded to each contestant not seriously injured) varied from 0 for a contest of maximum length, to +20 for a very short contest. The contest example shown earlier was one of the 2,000 Prober-Retaliator versus Prober-Retaliator contests.

Table 1 shows the average pay-off to each contestant in each type of contest. The number in a given row and

column is the pay-off gained by the row strategy when the opponent uses the column strategy. For example, in contests between Mouse and Hawk, the average pay-offs are 19.5 to Mouse and 80.0 to Hawk.

To tell whether a strategy is evolutionarily stable against the other four strategies, we examine the corresponding column in Table 1. For example, for Hawk to be an ESS, it is necessary that it be the most profitable strategy in a population almost entirely of Hawks. In such a population, a given animal of any type will almost always have a Hawk as opponent. Therefore the pay-offs in the "Hawk" column apply. These show that Mouse and Bully are both more successful than Hawk. Therefore natural selection will cause alleles for Mouse and Bully behaviour to increase in frequency, and alleles giving Hawk behaviour to decrease. Thus Hawk is not an ESS.

Examining the other columns, we see that Mouse is not an ESS because Hawk, Bully, and Prober-Retaliator average higher pay-offs in a population almost entirely of Mouse. Nor is Bully an ESS. However, Retaliator is an ESS since no other strategy does better, though Mouse does equally well. And the last column shows that Prober-Retaliator is almost an ESS.

How would we expect such a population to evolve? It will come to consist mainly of Retaliators or Prober-Retaliators, with the other strategies maintained at a low frequency by mutation. The balance between the two main types will depend on the frequency of Mouse, since the habit of probing is only an advantage against Mouse. For the particular values in Table 1, it can be shown that if the frequency of Mouse is greater than 7%, Prober-Retaliator will replace Retaliator as the predominant type. It is worth noting that a real population would contain young, senile, diseased and injured individuals adopting the strategy Mouse for non-genetic reasons.

Thus the simulation shows emphatically the superiority, under individual selection, of "limited war" strategies in comparison with the Hawk strategy.

Briefly, the reason that conflict limitation increases individual fitness is that retaliation behaviour decreases the fitness of Hawks, while the existence of possible future mating opportunities reduces the loss from retreating uninjured.

This general result will not be altered by moderate changes in the program parameters, though very large changes will alter it. One way would be by changing the probability of serious injury from a single *D* from 0.10 to 0.90. This would give advantage to "Pre-emptive Strike" policies, making Hawk an ESS. (Such species are probably rare, because excessively dangerous weapons or tactics would be opposed by kin selection.) Another way to make selection favour "total war" behaviour would be by giving the same pay-off penalty for retreating uninjured as for serious injury. This would correspond to a species where an individual fights only a single battle in its lifetime, on which its reproductive success entirely depends. Our choice of +60 for winning, 0 for retreating uninjured, and -100 for serious injury represents a species where males have more than one opportunity to gain a mate. Changing these values to +60, -100, and -100 respectively, would make Hawk the optimal strategy. Conversely, +60, 0,

Table 1 Average Pay-offs in Simulated Intraspecific Contests for Five Different Strategies

		Opponent				
		"Mouse"	"Hawk"	"Bully"	"Retaliator"	"Prober-Retaliator"
Contestant receiving the pay-off	"Mouse"	29.0	19.5	19.5	29.0	17.2
	"Hawk"	80.0	-19.5	74.6	-18.1	-18.9
	"Bully"	80.0	4.9	41.5	11.9	11.2
	"Retaliator"	29.0	-22.3	57.1	29.0	23.1
	"Prober-Retaliator"	56.7	-20.1	59.4	26.9	21.9

—500 would represent a long-lived species with numerous opportunities to gain mates, where individual selection would still more strongly favour cautious strategies.

Real Animals

Real animal conflicts are vastly more complex than our simulated conflicts. (An interesting study by Dingle¹⁵ shows that this holds true even at the lowly level of the mantis shrimp.) Probably our models are true to nature in emphasising a category distinction rather than an intensity distinction between "conventional" and "dangerous" tactics. In real animals, however, there exist not only the category distinction, but also individual differences in the intensity and skill with which each kind of tactic is employed. Also, in many species there are several categories of increasingly dangerous tactics, instead of only one.

The advantage from making a category distinction is that this simplifies behavioural requirements for limited conflict. It is probably easier for genetics to program a snake not to use fangs at all in certain situations than to program it to use fangs as intensively as possible up to intensity k , but not at intensities greater than k . Similarly, fair and foul blows are distinguished in boxing, and conventional and nuclear weapons in war.

Under the condition that any act of physical aggression is treated as a D act, the theoretical model will result in symbolic fighting by threat from a distance. This would be advantageous for a species that has an inherent difficulty in fighting physically at a safe level. For example, domestic and wild cattle, which have very dangerous horns and are somewhat clumsy in their charges, make much use of threat displays (stomping, pawing, bellowing). The model will not, however, give rise to conflict behaviour that is wholly symbolic and never backed up by physical aggression or other sanctions, since such behaviour would not be evolutionarily stable without some mechanism reducing the reproductive success of mutant individuals deficient in responding to the symbols. An interesting problem is how the felids, with their dangerous teeth and claws, limit their physical combats to non-fatal levels. Probably the explanation is that they have a hierarchy of many conflict categories and limit their probing to small escalations. Consequently, it takes repeated escalations to raise the conflict to the most dangerous level.

In most animal species there is probably a high correlation between prowess in C tactics and in D tactics. This means that C level conflict provides information to each animal about how its opponent is likely to perform if the conflict is escalated. This permits improvement in strategies over those used in the computer model. Instead of probing at random, an animal will be more likely to probe if its opponent is inferior in conventional fighting. On the other hand, if its opponent is very superior in conventional tactics, an animal will frequently retreat without waiting for its opponent to try a probe. Thus actual animals may combine Prober-Retaliator and Mouse capabilities.

If animals can adopt different strategies according to the opponent that confronts them, then an interesting possibility appears. The "Hawk" column of Table 1 shows that the best strategy against a Hawk is Mouse: that is, retreat immediately. If a species includes deviant individuals who follow the Hawk strategy and fight recklessly against every opponent, then it will be advantageous for ordinary members of the species to be able to estimate recklessness and avoid combat with Hawks. But if this happens, then it will be advantageous to simulate wild, uncontrollable rage. And in fact the threat displays of some species do have an appearance of maniacal fury, hence there probably is some advantage in acting this way. However, if most species members simulate insane rage when actually their fighting is limited and controlled, then selection will favour indi-

viduals who partly discount the threat displays, and "call the bluff" of the pseudo-Hawks.

This leads to the suggestion that it might be advantageous for an individual animal to be maniacal in an easily recognisable way that could not be counterfeited. A possible instance of this is the phenomenon of going "on musth", which occurs periodically in adult male elephants^{16,17}. The temporal glands secrete a dark brown fluid that runs down the face, giving a visual and olfactory sign that cannot be counterfeited. The madness of the animal "on musth" causes other elephants to avoid him, and this may give an increase in dominance status that persists for a time after the musth period is over.

Conflict in which Injury is Impossible

The previous section offers an explanation of why, in a species with offensive weapons capable of inflicting serious injury, escalated fighting may be rare or absent. In doing so, it raises a second problem. In a contest between opponents who are unable to inflict serious injury, victory goes to the one who is prepared to continue for a longer time. How are such contests decided?

Suppose that the pay-off to the victor is v . If a contest is ever to be settled, there must also be some disadvantage to the contestants in a long contest. If so, the only choice of strategy open to a contestant is of the period for which he is prepared to continue, and hence of the pay-off, say $-m$, he is prepared to accept. Thus if two contestants adopt strategies m_1 and m_2 , where $m_1 > m_2$, the pay-off to the first is $v - m_2$ and to the second is $-m_2$. Our problem then is how a contestant should choose a value of m , or, more precisely, whether there is a method of choosing m which is an ESS.

To answer this question, we need a more precise definition of an ESS. We define $E_J(I)$ as the expected pay-off to I played against J . Then I is an ESS if, for all J , $E_I(I) > E_I(J)$; if for any strategy J , $E_I(I) = E_I(J)$, then evolutionary stability requires that $E_J(I) > E_J(J)$. The relevance of the latter condition is as follows. If in a population adopting strategy I a mutant J arises whose expectation against I is the same as I 's expectation against itself, then J will increase by genetic drift until meetings between two J 's becomes a common event.

It is easy to show that no "pure" strategy (that is, no fixed value of m) is an ESS. Thus in a population adopting strategy m , a mutant adopting $m + \epsilon$ would always do better (and if $m > v$, a mutant adopting a zero strategy would also do better). It is, however, possible to find a mixed strategy which is an ESS. Let strategy I be a mixed strategy which selects a value of m between x and $x + \delta x$ with probability $p(x)\delta x$.

Then if

$$p(x) = (1/v)\exp(-x/v) \quad (1)$$

it can be shown that I is an ESS.

We conclude that an evolutionary stable population is either genetically polymorphic, the strategies of individuals being distributed as in equation (1), or that it consists of individuals whose behaviour differs from contest to contest as in (1). There is no stable pure strategy, and hence no behaviourally uniform population can be stable.

Conclusions

There are many complications left out of these simple models. The analysis is, however, sufficient to show that individual selection can explain why potentially dangerous offensive weapons are rarely used in intraspecific contests; a stable strategy does, however, require that contestants should respond to an "escalated" attack by escalating in return. Also, if contests are settled by a process of attrition, then evolutionary stability requires that the popula-

tion be genetically polymorphic, or that individuals vary their behaviour from contest to contest.

A more detailed analysis will be published elsewhere.

Ideas similar to those described here have been applied to human neurotic behaviour by J. S. Price¹⁸.

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Lithospheric Plate Motion, Sea Level Changes and Climatic and Ecological Consequences

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We demonstrate quantitatively that the world-wide Mid to Upper Cretaceous transgression and subsequent regression may have been caused by a contemporaneous pulse of rapid spreading at most of the mid-oceanic ridges between -110 to -85 m.y. The rapid spreading caused the ridges to expand and hence reduced the volumetric capacity of the basins. The subsequent regression was caused by a reduction in spreading rates beginning at -85 m.y.

THE global nature of the great marine transgressions and regressions such as occurred in the Upper Cretaceous has been recognised for nearly a century¹. These fluctuations of sea level have been variously attributed to gradual filling of ocean basins by detritus displacing water onto the continents, down faulting of ocean basins to cause regressions¹ and simultaneous vertical movements of both continents and ocean basins^{2,3}. The transgressions and regressions have been linked to orogenic cycles; it has been argued² that during intervals of low orogenic activity reduced horizontal compression caused continental subsidence relative to sea level, hence transgressions, and that conversely orogenic episodes produced increased horizontal compression, increased continental elevation and marine regression⁴. Late Cainozoic sea level changes are certainly attributable to glaciation, but this cause is not applicable to the Upper Mesozoic.

Changes in the volume of ocean basins could explain flooding of portions of continental surfaces. It has been

proposed⁵⁻⁷ that such changes occur due to alterations in the volume of the mid-oceanic ridges. Valentine and Moores⁵ linked these volumetric changes to the assembly and breakup of super continents. Hallam⁸ speculated that the Upper Cretaceous transgression and regression may have been caused by a contemporaneous pulse of rapid spreading which substantially increased the volume of the world ridge system. We show that this latter proposal is correct.

Cause of Upper Cretaceous Transgression

The lithosphere formed at a spreading ridge axis is initially hot and therefore elevated; as it moves away from the axis, it cools and subsides^{9,10}. This cooling and subsidence is time dependent¹¹; the depth to which any portion of flanking-crust has subsided is essentially a function of age only. So one empirical age-depth relation fits most ridges regardless of spreading rate¹¹ (Table 1). Therefore, the volume of any ridge is a function of its spreading rate history and changes in the spreading rate cause, in time, changes in ridge volume. (It has been suggested that the axial portion of fast spreading ridges is deeper than that of slow spreading ridges¹¹; however, subsequent analysis has shown that this is not systematically true¹².) Larson and Pitman¹³ correlated anomaly lineations of Middle and Upper Mesozoic age in the Atlantic and Pacific. They calibrated these lineations with Deep-Sea Drilling Project data, thereby extending the magnetic polarity time scale to -160 m.y. From the geometry of these lineations they showed that during the Upper Cretaceous (-110 m.y. to -85 m.y.) there was an episode of rapid spreading in the central and south Atlantic and the Pacific. The geological evidence suggests an initial rise of sea level that began at or before the boundary between Upper and Lower Cretaceous (-100 m.y.), the cresting of this rise some time between the Turonian and Lower Maastrichtian (-90 and -70 m.y.) and a withdrawal that was most pronounced in the Maastrichtian but continued into the Cainozoic¹⁴⁻¹⁷.

Table 1 Empirical Values showing the Relationship between Crustal Age and Ridge Elevation¹¹

Age m.y.	Mean depth corrected (m)	Standard deviation (m)	No. of values	Mean depth at 5 m.y. intervals (m)	Elevation above 5.5 base level (m)
0	2,644	±109	40	2,644	2,856
2	2,948	±93	46		
4	3,178	±96	46		
5				3,243	2,257
6	3,309	±94	33		
8	3,480	±81	32		
10	3,545	±155	51	3,545	1,955
15				3,788	1,712
20				4,029	1,471
21	4,078	±33	33		
25				4,205	1,295
29	4,332	±17	17		
30				4,371	1,129
33.5	4,507	±77	13		
35				4,556	944
38	4,655	±46	27		
40				4,718	782
45				4,879	621
50				5,041	459
53	5,137	±47	20		
64	5,432	±100	15		
69.3				5,500	0
77	5,600	±63	13		

We use the Upper Cretaceous system of ridges proposed by Larson and Pitman¹³ (Fig. 2a, Table 3). In the Atlantic this system has not altered significantly since -180 m.y. except to extend both northwards and southwards. The Pacific ridges, however, are today different from the Cretaceous configuration¹³ (Fig. 2, a and c). For example, the lineations of Mesozoic age form a double magnetic bight indicating that a ridge-ridge-ridge triple junction must have existed at that time at points A and B of Fig. 2a. This system of ridges evolved into the present system (Fig. 2c). The Phoenix plate is now the Antarctic plate and Juan de Fuca, Cocos and Nasca plates are all that remain of the Farallon plate; the Kula plate is gone. The Galapagos Ridge (between the Cocos and Nasca plates) is no more than 10 m.y. old and does not affect our computations. Beginning at -75 m.y. there was a phase of spreading at about 3 cm yr⁻¹ between the small remaining eastern fragment of the Kula plate and the Pacific plate. (This event yielded the "Great Magnetic Bight of the North-east Pacific"¹⁸.) By -38 m.y. at the latest this spreading had ceased and the entire Kula plate with its bordering ridges had been subducted¹⁹. The volumetric increase due to this brief episode would have been small.

In calculating the volumetric changes for each interval, we have kept the length of each ridge segment fixed. In reality, the length of the ridges changed with time, but

Table 2 The Calculated Volume of the Ridge Segments at Various Times is Given as are the Changes in Total Volume and Sea Level

	-110	-100	-90	-85	-80	-70	-60	-50	-40	-30	-20	-10	
PAC-PH	24.2	44.3	59.0	64.9	57.5	47.5	39.1	32.6	26.3	22.0	20.0	19.4	Volume × 10 ⁶ (km ³)
PH-FAR	21.8	35.7	45.9	50.0	42.9	33.0	24.9	18.6	13.1	9.4	7.6	7.3	
PAC-FAR	26.7	43.7	56.1	61.1	57.7	53.7	48.2	44.6	39.1	37.1	35.8	35.6	
KUL-FAR	36.4	59.5	76.4	83.3	78.7	71.9	65.8	60.9	53.3	50.6	48.8	48.5	
PAC-KUL	51.8	49.4	44.7	43.4	35.6	23.6	14.6	7.9	3.8	1.3	0.1	0	
A-NA	6.5	10.6	13.6	14.8	14.8	14.7	14.5	14.3	13.6	13.2	13.0	12.9	
A-SA	0.0	11.5	20.0	23.4	22.6	21.5	20.1	19.3	16.7	15.3	14.6	14.6	
E-NA					2.0	5.0	7.3	9.0	10.2	10.9	11.2	11.3	
$\Delta V \times 10^6 \text{ km}^3$		85.4	148.2	173.7	144.9	102.8	67.5	40.0	9.7	-5.6	-14.3	-15.7	
$h-d \text{ m}$		212	362	421	354	254	168	100	24.0	-14.0	-33.0	-40.0	

Data and Computations

We have computed the volume of most of the mid-oceanic ridge system at several times, beginning in the Cretaceous and extending to the upper Tertiary (Table 2). For each time and for each ridge segment an average cross-sectional area was computed using a standard age-depth curve¹¹ (Table 1). The data are referred to present day sea surface. Since sea level varies with time it is more meaningful to consider ridge volume in terms of elevation above an abyssal reference plain of 5,500 m. A history of spreading rates for the ridge segments is adapted from Larson and Pitman¹³ (Table 3).

Table 3 Lengths and Half Spreading Rates of Ridge Segments from -110 m.y. to -9 m.y.

	Length of ridge (km)	Half spreading rates (cm yr ⁻¹)		
		Prior to 110 m.y.	110-85 m.y.	85-10 m.y.
Pacific-Phoenix (PAC-PH)	3,300	5	18	4
Phoenix-Farallon (PH-FAR)	4,950	3	9	1
Pacific-Farallon (PAC-FAR)	6,050	3	9	4
Kula-Farallon (KUL-FAR)	8,250	3	9	4*
Pacific-Kula (PAC-KUL)	8,800	4	3	0
Africa-North America (A-NA)	4,400	1	3	2
Africa-South America (A-SA)	4,950	0	5	2
Europe-North America (E-NA)	3,850	0	0	2
Total	45,550			

we assume that as some ridges have grown in length an equivalent volume of other ridges has been subducted.

The Indian Ocean and Tethys Sea have been left out of our calculation. The spreading of the Indian Ocean is known in sufficient detail¹⁰ but since the Tethys is gone its history cannot be determined. As a first approximation we assume that as Tethys closed due to the drift of various Gondwana fragments into Eurasia, any ridge system that existed in Tethys gradually subsided, ridges and ridge axes were subducted. We also assume that this consequent volumetric decrease was about equal to the simultaneous volumetric increase in the ridges of the Indian Ocean.

To convert changes of ridge volume into changes of continental freeboard, we calculated isostatic adjustment due to increased water depth. If water depth increases by a thickness h , oceans subside a distance d . Assuming 3.3 g cm⁻³ for the density of the upper part of the mantle, $h=3.3d$ and the change in freeboard will be $(h-d)=0.7h$.

A second correction arises because the boundaries of the oceans are not vertical. As the oceans rise, more surface area is covered (Fig. 1). Approximately 1/6 of the Earth's surface ($85 \times 10^6 \text{ km}^2$) lies at elevations between 0 and +500 m (ref. 20). We assume that as sea level rises the area covered by the sea increases linearly ($0.170 \times 10^6 \text{ km}^2$ for each 0.001 km rise in sea level). Thus, the change in continental freeboard $(h-d)$ may be calculated from the equation

$$V = hA_0 + (0.7h)^2 170/2$$

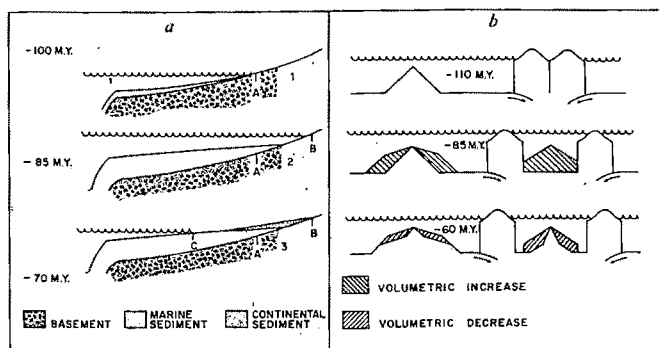


Fig. 1 *a*, Schematic Upper Cretaceous two ocean ridge system. As spreading rates increase at -110 m.y. ridges expand horizontally causing a transgression by -85 m.y. Decrease in spreading rates after -85 m.y. causes ridges to contract and the seas to withdraw. *b*, As sea level rises from -100 m.y. (A) to -85 m.y. (B), sediments fill and level the inland seafloors. In contrast, as sea level lowers an equivalent amount between -85 and -70 m.y., the area of continent exposed is much greater (curve B to C).

where A_0 is the surface area of the ocean at -110 m.y. and $(0.7h)^2/170/2$ is the volume occupied by the sea encroaching on the continent. Hallam⁸, using the data of Termier and Termier²¹, shows that $33 \times 10^6 \text{ km}^2$ of presently emergent crust was covered by seas at -110 m.y. The present area occupied by the oceans is $359 \times 10^6 \text{ km}^2$; thus the oceanic area at -110 m.y. was $392 \times 10^6 \text{ km}^2$. The freeboard change ($h-d$) has been calculated from the equation for each cumulative total change in volume.

The values of ($h-d$) given in Table 2 have been computed relative to sea level taken as zero at -110 m.y. But since $33 \times 10^6 \text{ km}^2$ of the present day land area was covered by the seas⁸ at that time we estimate (using a standard hypometric curve²⁰) that sea level was about 100 m higher than today. The curve in Fig. 3 has been adjusted to give sea levels relative to the present.

Estimates of the late Mesozoic-Cainozoic changes in sea level computed from our model agree well with other estimates based on outcrops of marine sediments (Fig. 3). All except Termier and Termier²¹ place the time of the maximum transgression at about -85 m.y. Our curve indicates that sea level 10 m.y. ago was 40 m above the present stand. The total present continental ice volume, most of which accumulated during the past 10 to 20 m.y., is equivalent to 60 m of sea level change²². Therefore, our model predicts a present day sea level within 20 m of that observed.

Our estimates differ from those inferred geologically by others²¹⁻²³ in two respects (Fig. 3). First, we obtain higher sea levels during the maximum transgression. Our calculation may contain errors inherent in our assumptions but the corresponding geological estimates of past marine transgressions are based on the extent of Upper Cretaceous marine sediments, and hence are low, since 70 m.y. of erosion must have removed some of the Upper Cretaceous deposits⁷. Second, our model predicts that the rise of sea level during the transgression will occur at about the same rate as the fall during the regression.

Some geological data point to a more rapid regression than transgression. But it is likely that sedimentation led to the continuous filling and levelling of the epicontinental seafloors. Therefore, depths of the Cretaceous epicontinental seas in general would have been less than 500 m, perhaps only 100 to 200 m as suggested by the limited palaeontological evidence²⁴. Consequently, the area drained by the first 200 m drop of sea level would have been very large relative to the area flooded by the latest 200 m rise of the transgression (Fig. 1*b*). We estimate that between -85 m.y. and -60

m.y. sea level would have fallen by more than 250 m. This would have been sufficient to drain most continental areas and is in agreement with geological evidence.

Consequences of our Model

What is the relationship between tectonism, climate change and fluctuations in faunal diversity? We believe that our

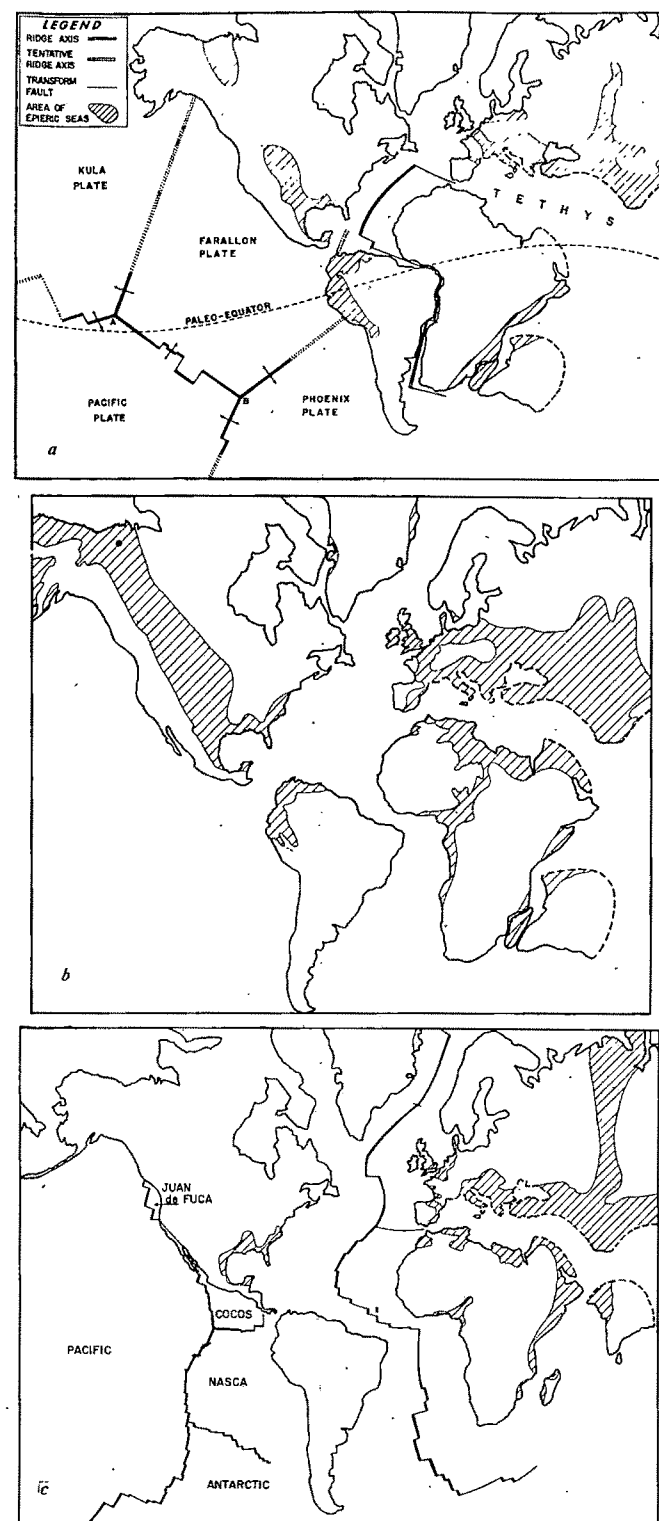


Fig. 2 The extent of the seas for three geological epochs^{14,16,17,21}: *a*, Cenomanian (-100 to -94 m.y.); *b*, Santonian-Campanian (-70 to -85 m.y.); *c*, Eocene (-50 to -40 m.y.). The arrangement of the ridge axes at present is shown in *c*, where they are plotted with respect to North America.

model provides a working hypothesis to connect these phenomena. The effects of the Upper Cretaceous transgression and regression on climatic, stability, faunal diversity and ocean circulation (Fig. 4) are not necessarily newly discovered relationships. But we discuss them briefly to emphasize that all are related to changes in the rate of plate motion.

World climate: The uniformity and relative mildness of climate at the height of the Upper Cretaceous transgression are well documented²⁵⁻²⁷. An increase in the ratio of oceanic to continental area moderates and stabilizes climate⁴. This is because the heat capacity of water is very large compared with continental rocks or the atmosphere. With more than 40% of the continents covered by several hundred metres of water, this moderating effect must have been large. Also, the expanse of the epicontinental seas provided new corridors along which heat could be advectively transferred between low and high latitudes. Conversely, as the seas withdrew beginning in the Upper Cretaceous, continentality increased probably producing the well documented high latitude cooling and increased seasonal contrasts that continued through the Tertiary. This cooling trend leads to polar glaciation in the mid-Tertiary²⁸ and mid-latitude glaciation in the Quaternary. Palaeomagnetic data³⁶ demonstrate that the Arctic Ocean and possibly Antarctica had drifted to a polar position by the Upper Cretaceous^{30,36}. We therefore attribute these Late Cretaceous glaciations to continued fall of sea level (which caused increasing emergence of all continents, including Antarctica) and increased constriction of oceanic thermal advection between low latitudes and the Arctic Ocean. Post-Cretaceous opening of the North Atlantic did not significantly improve circulation with the Arctic because, as the Atlantic opened, routes to the Pacific closed³¹.

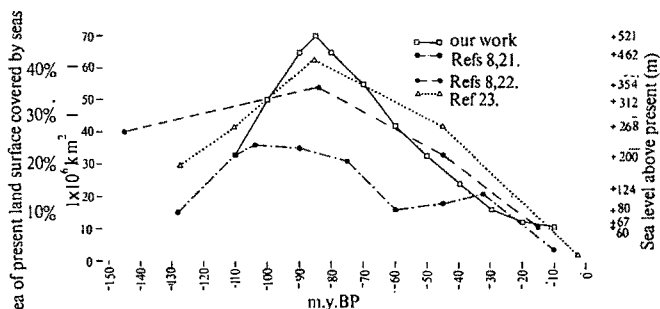


Fig. 3 Area of present day land covered by former seas plus the height of these seas above present levels plotted against age (adapted from ref. 8).

Ocean circulation: All available evidence suggests that the Upper Cretaceous oceans and their epicontinental seas were well mixed and productive in spite of the low thermal gradient between poles and equator. The pattern of circulation is not known, but it was probably quite different from that of the present.

Today the deep circulation of the oceans is maintained by high latitude formation of dense water in restricted seas or shallow shelf areas. We expect that a similar mechanism operated in the Upper Cretaceous and the source areas for deep and bottom waters lay in some of the epicontinental seas. With the withdrawal of the seas at the close of the Cretaceous some or all of these source areas may have been drained. New source areas would develop as the polar regions cooled but there may have been a short but important interval of stagnation as one regime of deep circulation was replaced by another. If a brief period of stagnation did occur there is no evidence that it led to the development of anaerobic conditions in any of the ocean basins.

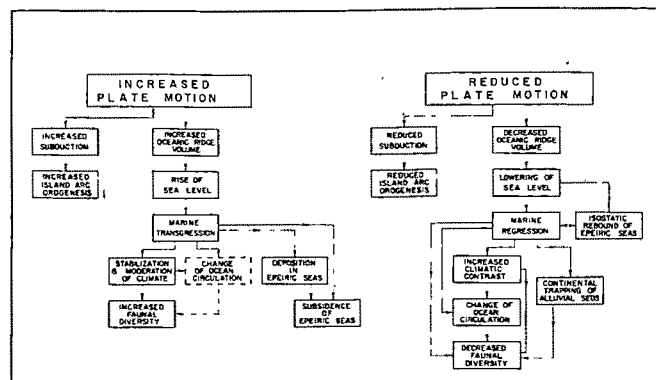


Fig. 4 Proposed sequence of events causally related to an Upper Cretaceous worldwide increase in the velocity of plate motion and subsequent decrease.

Mesozoic-Cainozoic faunal crisis: The Upper Cretaceous stable and uniform climates allowed significant increases in diversity of many groups^{32,33}. The adaptation to these conditions produced an inherent vulnerability to change³⁴. We conclude that the marine withdrawal was most rapid between -70 m.y. and -60 m.y. because of isostatic rebound and sediment infilling of epicontinental seas (Fig. 1). Thus, in latest Cretaceous, the land area would have nearly doubled. The consequent environmental changes (increased thermal gradients and seasonal contrast^{33,35} and marked alteration of the ocean circulation and thermal regime) were probably equally rapid, producing stresses on species adapted to stable Upper Cretaceous conditions.

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Possibilities for the Evolution of the Genetic Code from a Preceding Form

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Analysis of the interaction between mRNA codons and tRNA anticodons suggests a model for the evolution of the genetic code. Modification of the nucleic acid following the anticodon is at present essential in both eukaryotes and prokaryotes to ensure fidelity of translation of codons starting with A, and the amino acids which could be coded for before the evolution of the modifying enzymes can be deduced.

THE sequences of nucleotide bases in genetic DNA and in the corresponding mRNA molecules store inherited information which is translated into polypeptide chains of proteins by an adapter mechanism. This involves pairing between anticodons in tRNA molecules; carrying specific amino acids, and codons in mRNA. The rules of pairing between tRNA and mRNA molecules result in the genetic code (Table 1). Alterations in the nucleotide sequences of tRNA molecules produce functional changes. Two of the functions of tRNA that can undergo such changes are codon-anticodon pairing, the site for which is located in the anticodon loop, and amino acid recognition, which, seems to be determined by various components of the tRNA molecule, perhaps including its tertiary structure. In some tRNAs the amino acid acceptor stem is involved in synthetase recognition¹, but this rule does not hold generally, and Loftfield¹ has concluded that amino acid recognition appears to be a property of the tRNA molecule as a whole, and cannot be ascribed to any particular sequence of bases in it.

The anticodon is a sequence of three nucleotides next in sequence to an invariant uridine in the anticodon loop. Mutational changes in the anticodon can take place that change codon pairing without affecting amino acid recognition². Such mutations result in the 'wrong' amino acid being placed in many polypeptide sequences, and may therefore be expected to be deleterious or lethal. tRNA molecules can also undergo changes in both the anticodon and the amino acid recognition function and such 'double

changes' can occur during evolution. This was discovered by Squires and Carbon³ who found that a glycine tRNA in *Escherichia coli* was similar to a valine tRNA isolated from the same organism with, of course, a different anticodon and different amino acid recognition function. Similarity, in excess of the similarity between all tRNA molecules for different amino acids, was also noted for lysine and arginine tRNAs occurring in yeast⁴.

Anticodon-Codon Pairing

In this article I develop the thesis that part of the evolution of the genetic code is brought to light by examining the nature of anticodon-codon pairing and by examining the four nucleotides that comprise the anticodon in tRNAs that participate in polypeptide synthesis on ribosomes and the nucleotide next following. This is always a purine nucleotide or its modification.

Ambiguity in the pairing between the first base of anticodons and the third base of codons (termed here, for convenience, '1-3 pairing') is responsible for a definite pattern in the genetic code⁵. The ordered ambiguity in 1-3 pairing was elegantly interpreted by Crick⁶, as shown in Table 2, in the cases of I, G, U and C in position 1 of anticodons. He proposed that these bases pair with three, two, two and one bases respectively in codons. Similarly, the base G in the third codon position will pair with both U and C in position 1 of the anticodon. Ambiguous pairing between position 2 of anticodon and codon does not exist and, with one exception to be discussed below, does not exist between anticodon position 3 and codon position 1 (3-1 pairing). Non-ambiguous 3-1 pairing takes place between A and U, and G and C. This may be attributed to conventional hydrogen bonding. Pairing between G and U is, however, known to take place in various RNA sequences without hydrogen bonding, and without displacing the helical structure of double strands of RNA⁶. This concept is basic to the understanding of 1-3 pairing. The ambiguity in base pairing between G with U and C, and U with A and G, potentially enables thirty-two anticodons to suffice for translation of all the codons for amino acids, for each pair of codons represented by NNU and NNC can bind with an anticodon GNN, 'read' in the reverse direction, and each NNA and NNG codon pair can bind with anticodon UNN (Table 1). In addition, there are anticodons that provide for duplicate translation of codons; for example, the anti-

Table 1 The Genetic Code and the Identified Anticodons in Sequenced tRNAs

<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>	
GAA	UUU	Phenylalanine	IGA	UCU	Serine	GUA	UAU	Tyrosine		UGU	Cysteine
UAA	UUC	Phenylalanine		UCC	Serine		UAC	Tyrosine		UGC	Cysteine
CAA	UUA	Leucine	UGA	UCA	Serine	UUA	UAA	Chain Term.		UGA	Chain Term.
	UUG	Leucine		UCG	Serine	CUA	UAG	Chain Term.	CCA	UGG	Tryptophan
GAG	CUU	Leucine		CCU	Proline	GUG	CAU	Histidine	ICG	CGU	Arginine
	CUC	Leucine		CCC	Proline		CAC	Histidine	GCG	CGC	Arginine
	CUA	Leucine		CCA	Proline	UUG	CAA	Glutamine		CGA	Arginine
CAG	CUG	Leucine		CCG	Proline	CUG	CAG	Glutamine		CGG	Arginine
IAU	AUU	Isoleucine		ACU	Threonine		AAU	Asparagine	GCU	AGU	Serine
GAU	AUC	Isoleucine		ACC	Threonine		AAC	Asparagine		AGC	Serine
	AUA	Isoleucine		ACA	Threonine	UUU	AAA	Lysine	UCU	AGA	Arginine
CAU	AUG	Methionine		ACG	Threonine	CUU	AAG	Lysine		AGG	Arginine
IAC	GUU	Valine	IGC	GCU	Alanine	GUC	GAU	Aspartic acid	GCC	GGU	Glycine
GAC	GUC	Valine		GCC	Alanine		GAC	Aspartic acid		GGC	Glycine
UAC	GUA	Valine		GCA	Alanine	UUC	GAA	Glutamic acid	UCC	GGA	Glycine
	GUG	Valine		GCG	Alanine		GAG	Glutamic acid	CCC	GGG	Glycine

a=Identified anticodons; *b*=codons.

The bases in anticodons are shown in unmodified form, except for I (inosine) which is a modification of A. The modifications are listed in Table 2.

Anticodons starting with G pair with codons ending in U and C; those starting with I pair with codons ending in U, C and A, and so on, as shown in Table 2.

codons UCC and CCC in glycine tRNAs both bind with the GGG codon for glycine.

Recent research by Nishimura and others (reviewed in ref. 7) has extended the pattern of ambiguity in 1-3 pairing. Uridine 5-oxyacetic acid in the first position of anticodons in certain *E. coli* tRNAs pairs with either U, A or G in the third codon position, and 2-thiouridine pairs only with A and not with G (ref. 7). Such modifications thus can either increase or decrease the ambiguity in 1-3 pairing. These enzymatic modifications of base 1 in anticodons vary in different organisms, and so have originated during the evolution of such organisms.

The presence of the invariant U preceding the anticodon would impose the minimum amount of steric hindrance to 1-3 pairing. This presumably facilitates pairing between modified bases at anticodon position 1 and codon position 3. Below, we shall contrast this with the effect of the modifications of the nucleoside following position 3 of the anticodon.

Table 2 First Base of Anticodons in Sequenced tRNAs compared with Third Base of Codons Paired

First base in anticodon	Pairing with	Organisms (E=eukaryotes, P=prokaryotes)	In tRNAs for
H (I)	U, C, A	E, P	Ile, Val, Ser (UCN), Ala, Arg (CGN)
G	C, U	E, P	Phe, Leu (CUN), Ile, Val, Tyr, Asp, Arg (CGN), Gly, Ser (AGY)
Gm	C, U	E	Phe
G ⁺ ('Q')	C, U	P	Tyr, His, Asn, Asp
U	A, G	P	Gly, Term.
s ² U	A	E, P	Gln, Lys, Glu
oa ⁵ U	U, A, G	P	Val, Ser (UCN)
U ⁺	A, G (?)	E, P	Leu (UUR), Arg (AGR)
C	G	E, P	Leu (CUN, UUR), fMet, Gln, Lys, Trp, Gly, iMet
ac ⁴ C	G	P	Met
Cm	G	E	Trp

Abbreviations: H, hypoxanthine; I, inosine; oa⁵U, uridine-5-oxyacetic acid; Gm, 2'-O-methylguanosine; G⁺, 'Q-base' (an unidentified guanosine derivative); s²U, 2-thiouridine; U⁺, unidentified uridine derivative; ac⁴C, 4-acetylcytidine; Cm, 2'-O-methylcytidine; N, unidentified nucleoside; R, purine; Y, pyrimidine; fMet, N-formyl methionine; iMet=initiator methionine.

Adenine is absent in position 1 of anticodons. Adenine in this position is deaminated to hypoxanthine by a specific enzyme, adenine anticodon deaminase (ACD)⁸. Hypoxanthine, which is the base in the nucleoside inosine (I), pairs with U, C, and A (Table 2). Anticodons with I in position 1 can therefore exist for amino acids that have quartets of four codons that start with the same two bases (see, for example, the set of alanine codons in Table 1), but not for amino acids with two codons in a set (such as phenylalanine), because in the latter case, anticodons starting with I would transfer two different amino acids to the same codon. Anticodons starting with A, which should translate codons ending in U, therefore do not exist in living systems, and mutations that bring such anticodons into being in tRNAs for amino acids having two codons in a set are evidently discarded because the enzyme ACD presumably changes A in this position to I in any and all tRNA molecules. All tRNAs that have been sequenced which translate pairs of codons ending in pyrimidines have anticodons starting with G, when such pairs of codons are assigned to a single amino acid, provided that the corresponding pair of codons ending in purines is assigned to a different amino acid. This has been found so far for the tRNAs for Phe, Tyr, His, Asp and Ser (AGY codons).

Evolution of the Genetic Code

Various authors have advanced schemes for the origin of the genetic code based on proposals for direct affinity between amino acids and nucleotide bases or groups of bases. Such affinities are deemed to have played a part in the origin of life in the lifeless 'primitive soup'. The speculations are stimulated by experiments showing the formation of amino acids, purines and pyrimidines from mixtures of methane, hydrogen, ammonia, water, and so on, when treated with electrical discharge or ultraviolet radiation, as reported by Miller, Oro and others^{9,10}. The present genetic code, however, and presumably its immediate antecedents, involve the intervention of adapter molecules of tRNA which combine enzymatically with amino acids, rather than direct affinity between amino acids and nucleic acid molecules.

There are various possibilities for the composition of earlier codes. The number of amino acids coded may have been either more or less than twenty. Amino acids may have been added to the code during evolution or may have

disappeared. I have suggested that arginine displaced ornithine during the evolution of protein synthesis¹¹.

The idea that the number of amino acids in earlier codes was less than twenty is favoured by the fact that some of the 'simple' amino acids, such as serine, glycine and alanine, have four or more codons, and that the codons may be arranged in 'quartets', such as GCU, GCC, GCA and GCG for alanine, in which only the first two bases confer specificity on the amino acid. A code of 'quartets' of codons would suffice for not more than sixteen amino acids, and an arbitrary choice of 'newer' amino acids can be made¹² to reduce the present twenty to fifteen. Perhaps codons were not used for polypeptide chain termination. We shall now consider a different approach to identifying a smaller list of amino acids in the code, emphasising changes in anticodon-codon pairing.

Role of the Nucleotide following the Anticodons

Modifications in this nucleotide at RNA position 40 (ref. 13) are summarised in Table 3. The predominant pattern into which they fall shows that they are evidently concerned with establishing A-U and U-A pairing between the third anticodon position and the first codon position ('3-1 pairing'), occurring on the ribosome during polypeptide synthesis. These modifications enable the composition of a 'primitive' code for ten amino acids, six with eight codons and four with four codons, to be proposed.

Modifications at tRNA position 40 (Table 3) exist in both prokaryotes and eukaryotes. For 3-1 pairing between U and A, the modification in every known case consists of a bulky threonyl-containing side chain on position 6 of adenine. Presumably, these side chains serve, by steric

hindrance, to prevent pairing between U in the third position of the anticodon and G in the first position of the codon. The prevention of this pairing would be essential to fidelity of translation of all codons starting with A with the exception of *E. coli* tRNA^{Met}. This exception supports this hypothesis as follows: this tRNA initiates protein synthesis in *E. coli* by pairing with either AUG (the methionine codon) or GUG (a codon that normally is translated by valine). This tRNA has an unmodified A at position 40. Absence of the modification therefore permits 3-1 pairing by U with A or G and translation of either AUG or GUG as methionine. Uhlenbeck *et al.*⁶ examined the binding of GUG and a number of related oligomers by *E. coli* tRNA^{Met}. GUG and AUG had the same association constants with this tRNA. GUGA, which would bind with the sequence UCAU in the anticodon loop, had a much higher *K* than GUGU, suggesting that GUG in this oligomer was binding to the anticodon.

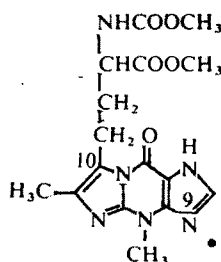
In the case of 3-1 pairing between A and U, the most common modification at position 40 is a bulky isopentenyl-containing side chain attached to adenine. An even more bulky molecular grouping, the large and complex 'Y-base', occupies position 40 in the eukaryotic phenylalanine tRNAs (for yeast, wheat and rabbit).

In the case of codons starting with U, it is essential that they should pair with anticodons ending with A and not with anticodons ending with G. These are anticodons for leucine (CUN codons), proline, histidine, glutamine and arginine (CGN codons). The nucleotide adjoining the anticodon in these tRNAs is methylated in prokaryotes (Table 3). Evidently, there is no 3-1 pairing between G and U, but always between G and C. Position 40 is often unmodified in tRNAs for amino acids with anticodons ending in C. This may be because there is no ambiguity in C-G 3-1 pair-

Table 3 Modifications of Nucleosides at Site 40 in tRNAs as Correlated with Recognition of Codons in *E. coli* (*E.c.*) and Yeast (*Ye*)

Codon	Nucleoside adjoining anticodon		Codon	Nucleoside adjoining anticodon		Codon	Nucleoside adjoining anticodon		Codon	Nucleoside adjoining anticodon	
	<i>E.c.</i>	<i>Ye</i>		<i>E.c.</i>	<i>Ye</i>		<i>E.c.</i>	<i>Ye</i>		<i>E.c.</i>	<i>Ye</i>
UUY	ms ² i ⁶ A	Y base	UCY		i ⁶ A	UAY	ms ² i ⁶ A	i ⁶ A	UGY	ms ² i ⁶ A	
UUA	ms ² i ⁶ A		UCA	ms ² i ⁶ A	i ⁶ A	UAA			UGA	—	
UUG	ms ² i ⁶ A	m ¹ G	UCG	ms ² i ⁶ A		UAG			UGG	ms ² i ⁶ A	A
CUY	m ¹ G		CCU			CAY	m ² A		CGY	m ² A, G	A
			CCC								
CUA			CCA			CAA	m ² A		CGA	m ² A	A
CUG	m ¹ G		CCG			CAG	m ² A		CGG		
AUY	t ⁶ A	t ⁶ A	ACU			AAU	t ⁶ A		AGY	t ⁶ A	
			ACC	mt ⁶ A,		AAA	t ⁶ A	t ⁶ A	AGA		t ⁶ A
AUA		t ⁶ A	ACA	t ⁶ A		AAG	t ⁶ A	t ⁶ A	AGG		
AUG	t ⁶ A		ACG								
AUG-f	A	t ⁶ A				GAY	m ² A	m ¹ G	GGY	A	
GUY	A	A†	GCY		meI	GAA	m ² A		GGA		
GUA	m ⁶ A	A†	GCA	A	meI	GAG	m ² A		GGG	A	
GUG	m ⁶ A		GCG								

Y-base, a guanosine derivative:



m¹G, 1-methylguanosine; meI, methylinosine; m²A, 2-methyladenosine; m⁶A, 6-methyladenosine; mt⁶A, N-methylcarbamoyl in t⁶A; i⁶A = 6-(Δ² isopentenyl)adenosine; t⁶A = N-(9-(β-ribofuranosyl)purin-6-ylcarbamoyl)-L-threonine*; ms²i⁶A, 2-methylthio-6-(Δ²-isopentenyl)adenosine; A†, unidentified adenosine derivative.

* Threonine-containing nucleosides were found in tRNAs accepting arginine and serine.

Table 4 Changes in Ancestral Code Leading to Present Code for Ten Amino Acids

(i) Ancestral Code for Ten Amino Acids

<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>	
NAA } NAG }	UUN	Leu	NGA } NGG }	UCN	Pro	RUA } RUG } YUA } YUG }	UAY	His	NCA } NCG }	UGN	Arg(Orn)
NAG	CUN	Leu	NGG	CCN	Pro	RUG } YUG }	CAY } CAR }	His } Gln }	NCG	CGN	Arg(Orn)
NAU	{ AUN GUN }	Val } Val }	NGU	{ ACN GCN }	Ala	RUU } YUU }	{ AAY } { GAY }	Asp }	NCU	{ AGN } { GGN }	Gly
NAC	GUN	Val	NGC	GCN	Ala	RUC } YUC }	GAY } GAR }	Asp } Glu }	NCC	GGN	Gly

(ii) Changes in (i) Leading to Code 2 as a Result of Enzymatic Modification of tRNA Base 40 and Consequent Suppression of U·G Pairing

<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>	
GAA } YAA }	UUY } UUR }	Phe } Leu }	NGA } NGG }	UCN } CCN }	Ser } Pro }	GUA } YUA }	UAY } UAR }	Tyr } C.T. }	NCA } NCG }	UGN } CGN }	Cys } Arg(Orn) }
NAG	CUN	Leu	NGG	CCN	Pro	GUG } YUG }	CAY } CAR }	His } Gln }	NCG	CGN	Arg(Orn)
NAU	AUN	Ile	NGU	ACN	Thr	GUU } YUU }	AAY } AAR }	Asn } Lys }	NCU	AGN	Ser
NAC	GUN	Val	NGC	GCN	Ala	GUC } YUC }	GAY } GAR }	Asp } Glu }	NCC	GGN	Gly

(iii) Changes in (ii) Leading to Present Code as a Result of Reassignment of tRNAs

<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>		<i>a</i>	<i>b</i>	
GAA } YAA }	UUY } UUR }	Phe } Leu }	NGA } NGG }	UCN } CCN }	Ser } Pro }	GUA } YUA }	UAY } UAR }	Tyr } C.T. }	GCA } UCA } CCA }	UGY } UGA } UGG }	Cys } C.T. } Trp }
NAG	CUN	Leu	NGG	CCN	Pro	GUG } YUG }	CAY } CAR }	His } Gln }	NCG	CGN	Arg
GAU } UAU } CAU }	UAY } AUA } AUG }	Ile } Ile } Met }	NGU	ACN	Thr	GUU } YUU }	AAY } AAR }	Asn } Lys }	GCU } YCU }	ACY } AGR }	Ser } Arg }
NAC	GUN	Val	NGC	GCN	Ala	GUC } YUC }	GAY } GAR }	Asp } Glu }	NCC	GGN	Gly

a, Anticodons; *b*, codons, showing anticodon-codon pairing in the first position of codons that includes ambiguity produced by pairing between G and U in addition to G·C and A·U pairing; (ii) code 2 is produced as a result of elimination of this ambiguity; (iii) present code resulting from changes in (ii).

ing, a result which would be consistent with the lack of ambiguity in C·G 1-3 pairing.

The pattern of modification at position 40 in the tRNAs of eukaryotes is less consistent than in prokaryotes. Perhaps eukaryotic ribosomes have assumed some of the functions needed for prevention of ambiguity. It is not known whether the initiator tRNA in eukaryotes pairs with GUG as well as with AUG.

All modifications of nucleotides in tRNA take place by enzymatic mechanisms following transcription. The evolutionary origin of the participating enzymes presumably antedated the prokaryote-eukaryote separation since, for example, t⁶A (Table 3) at position 40 occurs in all *E. coli* and yeast tRNAs that code for amino acids with codons starting with A. In an era before the evolutionary elaboration of these enzymatic modifications of position 40, 3-1 pairing in the ancestral prokaryotes would occur between U·G, and G·U as well as between A·U and U·A. Using only this assumption, and applying it to the present genetic code, an ancestral code results that contains eight codons apiece for each of six amino acids and four codons apiece for each of four amino acids (Table 4). It follows that the identity of these amino acids is such that their codons now start with C or G, and not with A or U. It is necessary, of course, to specify that each set of anticodons, or codons, can specify only one amino acid. As examples, the four codons for valine in the present code can be represented by GUN, pairing with anticodons represented by NAC. U·G pairing would, however,

codons NAU. These anticodons would pair also with the AUN codons. These must have been then assigned to valine, for the same set of anticodons would not specify two different amino acids. The initiator amino acid in protein synthesis by means of AUG and GUG codons would therefore have been valine.

The leucine codons CUN (Table 4) pair with anticodons NAG. The NAG anticodons will, however, also pair (G·U pairing in 3-1 position) with codons UUN, and these will also pair (A·U pairing) with anticodons NAA. Therefore, in this model, the CUN and UUN codons all coded for leucine.

The model for the ancestral code in Table 4 requires, for example, that proline, with anticodons NGG (pairing with codons CCN), should also have anticodons NGA, because NGG and NGA will both pair with codons UCN. Therefore UCN and CCN would be eight codons for proline. The codons with a middle A pose a special problem, for no amino acid has more than two codons with a middle A. It is therefore not possible to select, in terms of the present model, between histidine and glutamine, or between aspartic and glutamic acids, as to which member of each pair should be included in the ancestral code, so all four must be included. The procedure (Table 4, (i)) therefore leads to an ancestral code for ten amino acids.

These can be identified by their present codons all of which start with C or G. Arginine, for reasons advanced elsewhere¹¹, may have been preceded by ornithine. Therefore,

ancestral code. The inclusion of glutamine is surprising; this amino acid is formed enzymatically from glutamic acid. An alternative possibility is that all RUG, YUG, RUA and YUA anticodons belonged to histidine, and that the divergence between histidine and glutamine occurred during the later stage represented by Table 4 (ii).

It is of interest that yeast leucine-3 tRNA, with the anticodon CAA, pairing with UUG has 1-methylguanosine, that is, only a small side chain rather than an isopentenyl side chain, at position 40. This seeming anomaly is, however, consistent with the fact that specific distinction is not required between UUR and CUN codons, all six of which are for leucine (Table 4 (ii)). Therefore position 40 may have discarded 'bulky' modifications during the evolution of eukaryotic leucine tRNAs for pairing with codons starting with U.

The ten amino acids in the ancestral code would be adequate for the synthesis of proteins with reasonably versatile properties, except that the absence of serine is surprising. The list includes leucine and valine with hydrophobic side chains; the 'helix-breaker', proline; the two simple amino acids, alanine and glycine; histidine, which binds substrates and prosthetic groups; aspartic and glutamic acids, the acidic pair; a basic amino acid, ornithine; and glutamine, which is somewhat hydrophilic. According to the model, serine entered the code with eight codons, UCN and AGN, at the intermediate stage.

The expansion of the code to eighteen amino acids (Table 4 (ii)) was preceded by modifications of tRNA base 40, leading to the suppression of 3-1 pairing between G and U, and U and G. This enabled modifications of the amino acid recognition characteristics, by mutational base changes, to be adopted in tRNAs, so that 'new' amino acids entered

the process of protein synthesis, thus conferring novel and advantageous properties on proteins. Further expansion of the code to twenty amino acids then took place by other reassignments of tRNA molecules as summarised in Table 4 (iii). It is customary to postulate that a single species of organism, possessing the present code, displaced all other living organisms and proceeded, by divergent evolution, marked by gene duplication, allopatric speciation and natural selection, to give rise to various lines of descent that led to the existing terrestrial biota.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Satellite Observations of Intensity Variations of the Zodiacal Light

OBSERVATIONS of the intensity of the zodiacal light at 6530 Å have been made with a photometer on board the satellite D2A 'Tournesol'. This satellite was launched on April 15, 1971, from Kourou (French Guiana) into an orbit of inclination 46° with a perigee of 456 km and an apogee of 700 km. The spin axis was oriented towards the Sun with an accuracy of ~ 15 arc min and a spin period of 60 s (Fig. 1). The line of sight of the photometer is perpendicular to the spin axis and therefore scans the celestial sphere in a plane orthogonal to the ecliptic plane and to the direction of the Sun. Observations in a plane perpendicular to the Earth-Sun line (that is, at elongation $\epsilon = 90^\circ$ or $\epsilon = -90^\circ$) were carried out during the night phase, when the solar depression angle was $> 25^\circ$ and the altitude of the lowest observed points was > 135 km. Because of this, the signal contained no contribution from the night-glow, but was only due to zodiacal light and starlight. The data cover, without interruption, the period from April 19, 1971, to June 1973.

The photometer has been described previously¹. It has one channel at Balmer alpha (6563 Å), and a second at 6530 Å. Only 6530 Å data will be discussed here. The

bandwidth was 20 Å and the signal was integrated for $\frac{1}{8}$ s. Because of this integration time the field of view is extended from $1^\circ 20' \times 2^\circ 40'$ to $6^\circ 35' \times 2^\circ 40'$. A signal

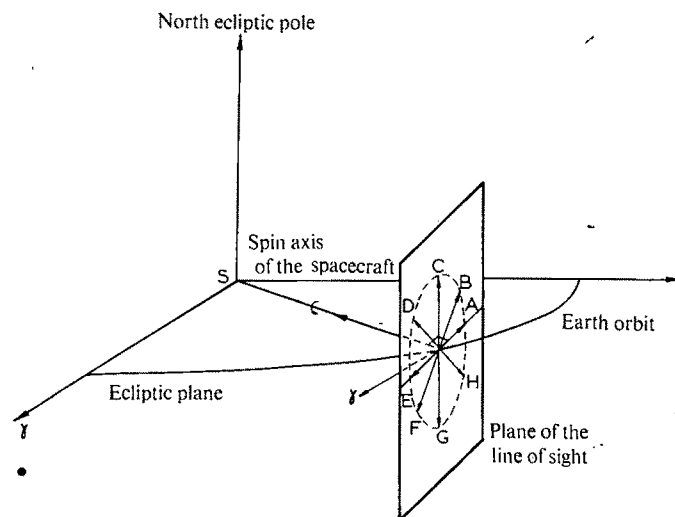


Fig. 1 Line of sight of the photometer. A, $\epsilon = 90^\circ$, $\beta = 0^\circ$; B, $\epsilon = 90^\circ$, $\beta = 45^\circ$; C, $\epsilon = 90^\circ$, $\beta = 90^\circ$; D, $\epsilon = 90^\circ$, $\beta = 45^\circ$; E, $\epsilon = -90^\circ$, $\beta = 0^\circ$; F, $\epsilon = -90^\circ$, $\beta = -45^\circ$; G, $\epsilon = -90^\circ$, $\beta = -90^\circ$; H, $\epsilon = 90^\circ$, $\beta = -45^\circ$. ϵ is $\pm 1^\circ 20'$; β is $\pm 3^\circ 20'$.

of 100 S_{10} (vis) provides a count rate of ~ 670 counts s^{-1} , compared with a dark current of 60 counts s^{-1} outside the South Atlantic anomaly. A star takes two days to cross the field of view because of the rotation of the Sun-spacecraft line. This allowed us to demonstrate that after taking into account variations of sensitivity across the field of view, no sensitivity change could be detected. Furthermore, the on-board calibration source gave a signal that was constant within $\pm 5\%$. We therefore believe that no short term fluctuations of the instrument response occurred during the 2 yr of observation. The instrumental arrangement thus allows a measurement of the zodiacal light and its variation from day to day.

Table 1 Points Ignored in Editing Data

Moonlight (arbitrary units)	New Moon				Quar- ter Moon				Full Moon	
θ	0	1	2	3	4	5	6	7	8	9
(Line of view, Moon direction)	25°	25°	25°	30°	40°	50°	60°	60°	70°	70°
	180°									

All data relevant to a field of galactic latitude less than 30° , or containing a known star of magnitude brighter than +6 or corresponding to the simultaneous observation on the 6563 Å channel of an HII region or of a non-nominal geocoronal Balmer α emission have been removed from this analysis. All points less than an angle θ from the Moon, given in Table 1, together with the Lagrangian points of the Earth-Moon system have also been removed. After this editing of the data, the recorded signal N was generally between 600 and 3×10^3 counts s^{-1} . The zodiacal light intensity is $I = (N - n)c/20 - h(I^{\text{II}}, b^{\text{II}})$ where n is the dark current, c the absolute calibration coefficient and $h(I^{\text{II}}, b^{\text{II}})$ the integrated starlight contribution² as a function of galactic coordinates. Two consecutive years of data have already been reduced.

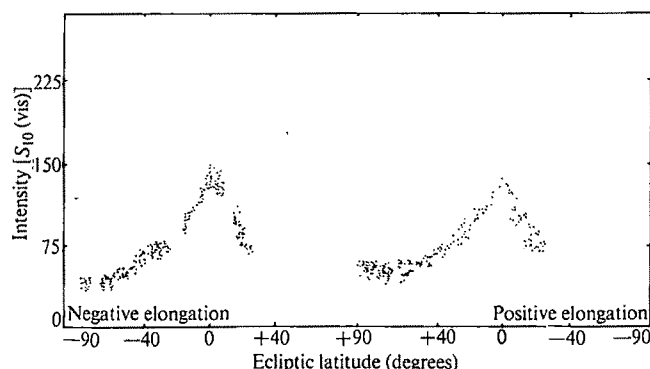


Fig. 2 Typical example of the 6530 Å intensity as a function of the ecliptic latitude β for May 25, 1971.

Figure 2 shows a typical example of the 6530 Å intensity measured as a function of the ecliptic latitude β for May 25, 1971. The measurements were taken over four nocturnal parts of orbits and about sixty rotations of the satellite around its axis. The intensity has two maxima as the line of sight intersects the ecliptic plane and two minima in the direction of the ecliptic poles. The small scatter of the data allows an intensity of the zodiacal light to be measured quite accurately. As was found using OSO-2 satellite data³ the zodiacal light intensity remained constant during successive orbits on one day.

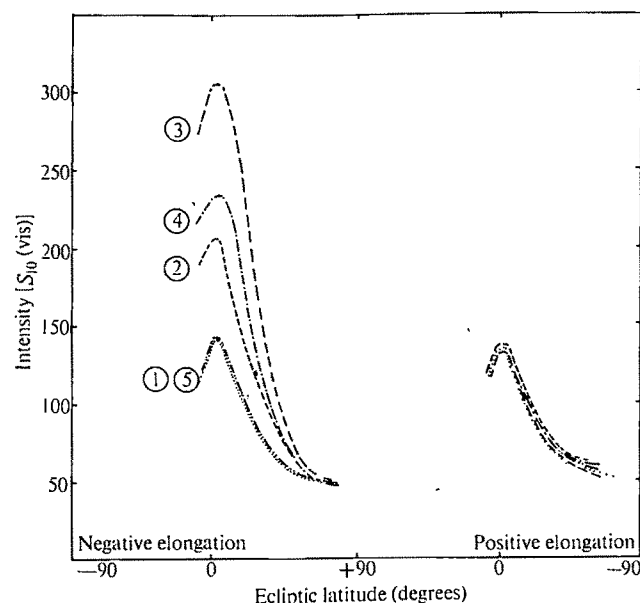


Fig. 3 Variation of the intensity of the zodiacal light. 1, November 4, 1971; 2, November 6, 1971; 3, November 7, 1971; 4, November 10, 1971; 5, November 12, 1971. Full Moon on November 2, 1971.

The intensity of the zodiacal light was sometimes observed (contrary to other satellite observations^{4,5}) to vary from one day to the next. Figure 3 shows an example of the variation of the intensity as a function of ecliptic latitude from November 5 to November 11, 1971. There was an increase of about 100% in the intensity for negative elongations, compared with the values on November 4 and November 12, while for the positive elongations it remained constant. To check whether the enhancements of the intensity were due to an asymmetry in the observations, measurements on November 4 were compared with those on November 7 under the same conditions: spacecraft latitude $\sim 45^\circ$, local time near midnight, no stray emissions, line of view above the horizontal plane of the spacecraft, and galactic latitudes comparable. Under those conditions, the enhancement was $\sim 100\%$.

Table 2 Comparison with Previous Measurements

β	Zodiacal light intensity at 90° elongation (S_{10} (vis))			
	Roach <i>et al.</i> ⁶	Dumont ⁷	Lillie ⁸	Our results
0°	250	202 to 170*	180	150 ± 10
45°	140	90 to 62*	75	75 ± 5
90°	110	65 to 50*	50	57 ± 5

* Lowest values.

To study the annual variation, the mean value of the intensities for eight directions (Fig. 1) (in the ecliptic plane, towards the ecliptic poles and at $\pm 45^\circ$ latitude) was computed for each day. The r.m.s. value was about $7S_{10}$ (vis). The number of measurements in each field is about fifteen, and the removal of a large proportion of data (to avoid stray emissions) is responsible for the fact that the eight mean values do not exist simultaneously on Fig. 4. When there is no increase, our results are in good agreement with previous measurements as is shown in Table 2. The main features of the data are the increases in intensity of up to 100% in a few days with a time constant of 3 to 25 d. The increases do not always appear simultaneously in all directions but may occur over a limited part of the sky.

The observations at the ecliptic poles are of considerable interest. Figure 5, which represents two consecutive years

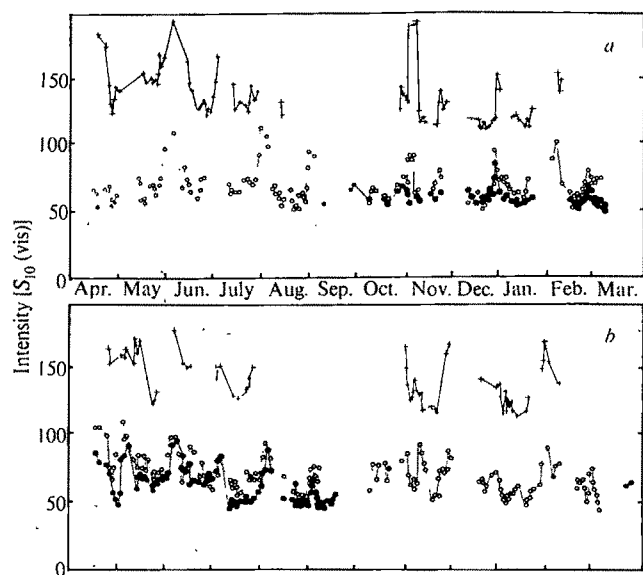


Fig. 4 Mean value of the intensity for eight directions (see Fig. 1). *a*, $\varepsilon < 0$: +, ecliptic plane (E); O, $\pm 45^\circ$ latitude (D, F); ●, south pole (G). *b*, $\varepsilon > 0$: +, ecliptic plane (A); O, $\pm 45^\circ$ latitude (B, H); ●, north pole (C).

of data, shows parallel trends of the evolution with time of the ratio of polar intensity to the intensity at 45° , and definitely proves that the variations of the zodiacal light are correlated with the position of the Earth in its orbit.

These variations may explain why the brightness of the zodiacal light is uncertain⁹ by a factor of ~ 2 . The large value of the variations and their dependence on angle of sight rule out an effect of the solar wind or of the solar activity.

In the example presented in Fig. 3, a 100% increase in intensity was observed near the ecliptic plane on November 7 and there was an enhancement of more than 50% for 6 d around the maximum. The Earth might not at that time have been far from the debris of comet Biela (Andromedids), the inclination of which to the ecliptic is 6° .

On April 21, an increase of 50% was observed in the polar and 45° directions and the half enhancement (25%) had been detected for 4 d. During this period the Earth encountered the Lyrids, the debris of comet 1861-I, the inclination of which is 80° .

It thus seems that the zodiacal light fluctuation by a factor of 2 is due to the scattering of solar light by local streams of particles. The variations in the increases as a function of angle to the ecliptic poles depend on the orbits of the particles. The magnitude of the increase would seem to indicate that the zodiacal cloud consists of a collection of such streams created on account of the Poynting-Robert-

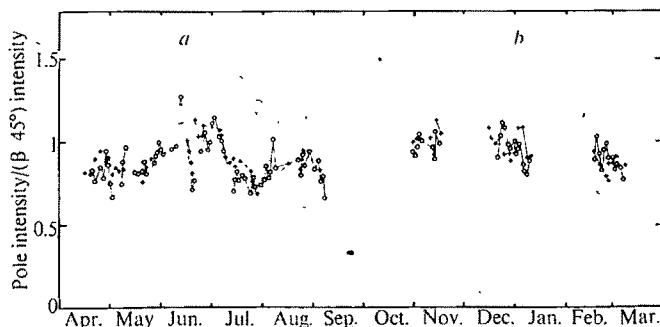


Fig. 5 Observations at the ecliptic poles in two consecutive years. O, April 1971 to March 1972; +, April 1972 to March 1973. *a*, North pole side; *b*, south pole side.

son effect by rather recent comets with a short lifetime. The interweaving of these elliptic toruses mainly constitutes the zodiacal cloud.

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New Galactic Supernova Remnants

We have identified twenty-seven galactic radio sources as supernova remnants by comparing 408 MHz observations from the Molonglo radio telescope and 5,000 MHz observations of comparable resolution from the Parkes 64-m radio telescope. The distribution of these and other supernova remnants with positions estimated from a new surface brightness-linear diameter relation has been investigated for evidence of galactic spiral structure.

Most extended non-thermal radio sources close to the galactic plane have morphological and spectral characteristics similar to those of the unambiguously identified galactic supernova remnants, and are consequently also considered to be supernova remnants (SNRs). These characteristics include: (i) a non-thermal radio spectrum, due to radiation by the synchrotron mechanism invoked to describe radio emission from SNRs; (ii) where resolution permits such recognition, a 'ring' or 'part-ring' radio brightness distribution indicative of an expanding shell source.

Within the region surveyed, seventy sources have previously been classified as SNRs (see ref. 1). Therefore the new observations represent a significant increase in the number of galactic SNRs observed at southern declinations, and in particular of older low surface brightness remnants for which previous lists were incomplete.

Green² has completed a high resolution 408 MHz galactic survey using the Molonglo telescope, which has a beamwidth of $2.86'$ in right ascension by $2.86'$ (zenith angle) in declination. The region with new galactic coordinates $|b| < 3^\circ$ and $l \ 195^\circ - 360^\circ - 55^\circ$ was observed. Because at 408 MHz non-thermal radiation predominates, the survey proved particularly useful for work on SNRs.

We prepared a list of those extended galactic sources from the Molonglo survey which had not previously been classified on the basis of their spectra and structure as HII regions, SNRs, or extragalactic radio sources. A cursory estimate of the spectral index was obtained using the 2,700 MHz flux densities from the Parkes survey (see ref. 3 and references therein); however, accurate spectral indices can best be obtained from investigations at two widely different frequencies with similar beamwidths. Accordingly, some seventy sources

which had been noted by Green² as worth investigating as possible SNRs from the 408 MHz–2,700 MHz comparison in the range l 260°–345°, plus some additional suspects outside this range, were observed with the Parkes 64-m radio telescope at 5,000 MHz (half-power beamwidth ~ 4 arc min). From the 408 MHz–5,000 MHz comparison we have been able to derive accurate positions, flux densities, spectral indices, and angular sizes for twenty-seven of these sources believed to be SNRs. Brightness temperature contour maps for the sources are in preparation, and will be presented separately.

For the 408 MHz observations the flux density scale used was that of Wyllie⁴. During each observing session several standard sources selected from Hundstead^{5,6} were measured for calibration purposes. At 5,000 MHz the system was calibrated using Hydra A for which a flux density $S(5,000 \text{ MHz})$ of 13.5 f.u. was assumed.

The derived parameters for the new remnants are given in Table 1, which includes the galactic source number ($l-b$), the equatorial coordinates (1950), the mean angular diameter and the flux densities and spectral index estimate for each source. The mean angular diameters $\langle \phi \rangle = (\phi_{\text{RA}} \times \phi_{\text{Dec}})^{1/2}$ were estimated from the outer radio isophotes used to determine the limits of integration in the estimation of the flux densities, and not from the half-power levels often used. The spectral index α is defined by the simple power law $S_\nu \propto \nu^\alpha$, where S_ν is the flux density at frequency ν . The flux densities for both 408 MHz and 5,000 MHz observations have errors due to noise and calibration uncertainties of less than 5%. The corresponding error in spectral index may be greater in confused regions where the extent of the source is not clearly defined. In such cases particular care was taken in defining the extent of integration. Sources with relatively flat spectra have been retained only where a thermal spectral index of -0.1 is believed to lie outside the range of possible errors. To exclude extragalactic objects, sources with relatively steep spectra have been excluded unless they show a shell structure.

Some properties of individual sources are as follows:

G321.9–0.3. This SNR extends into the error box of the Uhuru X-ray source⁷ 2U1516–56. But since the X-ray source is pulsating it is unlikely that the SNR itself is the origin of the X-ray emission.

G323.5+0.1. Since this non-thermal source is confused at 5,000 MHz with a neighbouring HII region, it has only been possible to place limits on the 5,000 MHz flux density.

G335.2+0.1. The proximity to the X-ray source 2U1624–49 may be worth further investigation.

G339.2–0.4. Although the spectrum of this source is not as steep as average ($\alpha_\nu = -0.48$) it seems to be non-thermal and has a part-shell structure. Its proximity to the X-ray source 2U1641–45 and the recently discovered Parkes pulsar 1641–45 is of interest.

If the relation between surface brightness Σ and linear diameter D for SNRs at known distances is established, the distances and galactic distribution of all others may be investigated if they are treated as being identical. Representing the relation as $\Sigma \propto D^{-n}$, earlier investigations of galactic SNRs have yielded empirical values of n in the range 2.7 (at 400 MHz, ref. 8) to 4.5 (at 1,000 MHz, ref. 1). Spectral and evolutionary differences, as well as observational errors, would be expected to have contributed to the uncertainty in n .

Mathewson and Clarke⁹ used fourteen SNRs detected in the Magellanic Clouds to establish the relation

$$\Sigma_{408} = D_{\text{pc}}^{-3} 10^{-15} \text{ W m}^{-2} \text{ Hz}^{-1} \text{ sr}^{-1}$$

This relation has the advantage that the distance of all the calibrators is reliably known, whereas for many of the galactic calibrators uncertainties in their distances of up to 50% exist. But as noted by Mathewson and Clarke⁹ the Magellanic Cloud SNRs seem to be inherently brighter objects than galactic SNRs of the same linear diameter.

In view of the uncertainties in earlier galactic Σ – D relations, and the apparent difference between Galactic and Magellanic Cloud SNRs, the galactic Σ – D relation has been rederived. The distance calibrators used were those class 1 and class 2 calibrators listed by Ilovaisky and Lequeux¹⁰ with surface brightness values in the range 3×10^{-21} to $3 \times 10^{-19} \text{ W m}^{-2} \text{ Hz}^{-1} \text{ sr}^{-1}$, this being the range over which we wish to apply the relation for distance determination. (We note that this excludes Cas A, the Crab, and Cygnus Loop.) The surface brightness results for the southern sources were calculated from the Molonglo survey.

Table 1 Parameters for the 'New' Remnants

Galactic source number	Position ($\sim$ centroid)		Mean angular diameter $\langle \phi \rangle$ (arc min)	Flux densities (f.u.)		Spectral index α	Distance d (kpc)	Displacement from galactic plane z (pc)
	RA (1950)	Dec. (1950)		408 MHz	5,000 MHz			
293.8+0.6	11 33 00	–60 36	19.4	9.0	2.1	–0.58	10.2	+107
296.0–0.6	11 48 15	–62 27	17.2	6.9	0.74	–0.89	11.6	–121
299.0+0.2	12 15 05	–62 11	21.3	12.6	4.7	–0.39	8.8	+31
302.3+0.7	12 42 40	–61 51	16.8	7.5	3.0	–0.36	11.3	+138
308.7+0.0	13 38 05	–62 01	12.3	16.7	7.0	–0.35	9.6	0
309.2–0.6	13 42 30	–62 37	12.8	10.0	3.9	–0.37	11.3	–118
309.8+0.0	13 47 05	–61 50	21.2	26.4	7.4	–0.51	6.9	0
315.4–0.3	14 32 00	–60 22	20.4	17.1	4.9	–0.50	8.1	–42
321.9–0.3	15 16 45	–57 29	24.8	18.3	7.8	–0.34	7.4	–38
323.5+0.1	15 25 05	–56 13	9.7	4.2	0.5 < S < 2.0	–0.8 < α < –0.3	16.6	+29
327.2–1.0	15 50 35	–54 56	16.3	10.6			10.2	–178
330.2+1.0	15 57 20	–51 25	11.1	8.6			12.4	+216
335.2+0.1	16 23 50	–48 36	18.6	27.1	8.6	–0.46	7.2	+12
337.2–0.7	16 35 45	–47 45	8.4	3.8	0.70	–0.67	17.9	–218
339.2–0.4	16 41 50	–46 03	10.8	7.5	4.5	–0.20	13.2	–92
340.4+0.4	16 43 00	–44 34	5.9	8.2	2.9	–0.41	15.4	+107
340.6+0.3	16 44 05	–44 30	4.1	7.0	2.8	–0.36	18.6	+97
344.7–0.1	17 00 15	–41 35	8.1	4.7	1.3	–0.51	16.9	–29
346.6–0.2	17 06 40	–40 06	12.3	14.9	4.3	–0.49	10.0	–35
350.0–0.3	17 17 35	–37 24	9.0	10.7	1.7	–0.73	12.4	–65
350.0–1.8	17 23 50	–38 18	37.9	49.5	13.6	–0.51	4.6	–144
351.2+0.1	17 19 05	–36 08	13.0	8.1	3.1	–0.38	12.1	+21
352.7–0.1	17 24 20	–35 05	11.9	9.6	2.3	–0.57	11.8	–20
355.9–2.5	17 42 30	–33 43	15.8	12.3	3.4	–0.51	9.8	–427
11.4–0.1	18 07 55	–19 06	13.6	5.3	2.8	–0.25	13.7	–24
15.9+0.2	18 16 05	–15 02	10.7	7.7	1.9	–0.56	13.1	+45
24.7–0.6	18 35 40	–07 36	16.7	12.3	3.6	–0.49	9.6	–100

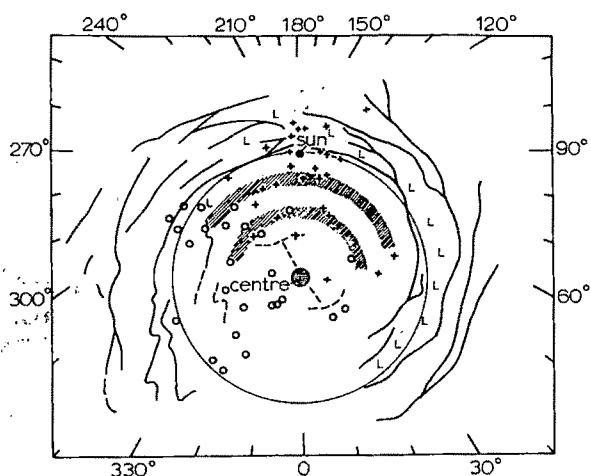


Fig. 1 Galactic neutral hydrogen map of Kerr¹¹, with SNR positions superimposed. The new SNRs are indicated by circles, and those from Woltjer¹² by crosses.

The data are well fitted by either of the expressions

$$\Sigma_{408} = 0.7 D_{pc}^{-3.0} 10^{-15} \text{ W m}^{-2} \text{ Hz}^{-1} \text{ sr}^{-1} \quad (1)$$

or

$$\Sigma_{408} = D_{pc}^{-3.11} 10^{-15} \text{ W m}^{-2} \text{ Hz}^{-1} \text{ sr}^{-1} \quad (2)$$

In expression (1) the Mathewson and Clarke exponent was retained. The difference in surface brightness could then indicate, as Mathewson and Clarke suggest, a mean initial energy for the Magellanic Cloud SNRs about 25% greater than that for galactic SNRs. In expression (2) the data were fitted retaining the Mathewson and Clarke proportionality constant and altering the exponent to fit the data, which might indicate a difference in evolutionary behaviour. But the difference in distance estimates for the two expressions over the Σ range of interest is less than 3%. We have arbitrarily adopted expression (1) for our subsequent calculations. SNR distance estimates thus obtained are about 10% less than those obtained using the Mathewson and Clarke relation, but somewhat greater than distance estimates obtained using earlier Σ - D relations. The distance estimates d , and displacement from the galactic plane z , for each of the newly discovered SNRs are included in Table 1.

The galactic distribution of the new SNRs catalogued in Table 1 is shown in Fig. 1 superimposed on the neutral hydrogen spiral arm map of Kerr¹¹. Kerr shows the two major arms within the solar circle (the Sagittarius and Norma-Scutum arms) as only roughly defined in view of the uncertainties in kinematic distances for this region. The position estimates of the new SNRs are indicated by circles. Also included on the diagram and indicated by crosses are the position estimates found using the new Σ - D relation, of the well known SNRs catalogued in Tables 1 and 3 of Woltjer¹² (with the exception of G8.5-0.3, which has been shown to be thermal¹³). The Crab, Cas A, and the Cygnus Loop are not included in the diagram since they have surface brightness values outside the limits used in deriving the Σ - D relation. SNRs with $|z| > 250$ pc have also been excluded from the diagram. Flux densities used in the distance calculations for the southern sources were taken from the Molonglo survey, while for those sources north of declination $+19^\circ$ data were taken from Woltjer¹².

The SNR distribution exhibits certain features similar to the HI distribution. Most of these SNRs lying between the Sun and galactic centre appear to lie on the inner spiral arms. The group of SNRs approximately 3 to 4 kpc from the galactic centre may indicate the position of the inner expanding arm (shown as dashed in Fig. 1).

More reliable distances for known SNRs are desirable in order to investigate the intrinsic dispersion of the Σ - D evolu-

tionary curve, and to see whether the technique of using SNRs as spiral arm tracers can be pursued further.

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Are Large Time Differences in Meteorite Formation Real?

In recent years two types of cosmochronological dating have been interpreted to indicate that there are large time intervals, a few times 10^7 yr, between the formation of various meteorite samples. For example, extrapolation backwards along isochrons in seven basaltic achondrites led Papanastassiou and Wasserburg¹ to establish a 'standard' initial $^{87}\text{Sr}/^{86}\text{Sr}$ ratio of 0.69898 ± 0.00003 (BABI ≡ 'basaltic achondrite best initial'). Similar isochrons in another basaltic achondrite, Angra dos Reis, led, however, to an initial ratio of 0.69884 ± 0.0004 (ADOR ≡ 'Angra dos Reis')². The difference between these two values is attributed to the accumulation of different amounts of the ^{87}Sr decay product of ^{87}Rb . If this reflects a difference in the times of fractionation between Rb and Sr in the meteoritic material, then the time interval is 14×10^6 yr. More recently, Tatsumoto, Knight, and Allegre³ found significant differences in the radiogenic $^{207}\text{Pb}/^{206}\text{Pb}$ ratios in Angra dos Reis and in two other basaltic achondrites, the value for Angra dos Reis being 0.6197 and the average of the other two being 0.6081. These nuclides result from the decay of ^{235}U and ^{238}U . If the differences are attributed to different times for the events of lead-uranium fractionation in the meteoritic materials, then the indicated time interval is 27×10^6 yr.

Are these time differences real? Or were there significant isotopic abundance variations in different parts of the primitive solar nebula in which different meteorite samples accumulated?

These questions are of obvious importance in establishing boundary conditions on the history of the Solar System. I present here a case for the second alternative and suggest experiments to settle the issue.

The isotopic composition of the heavier elements can vary if there is a variable ratio of s-process products to r-process products. These have different astrophysical sources. The s process probably takes place in stars somewhat more massive than the Sun while they are in their more advanced stages of evolution in the red giant region of the Hertzsprung-Russell diagram⁴. The products are probably ejected into space relatively gently in stellar winds or as parts of planetary nebulae; they cannot withstand unaltered the severity of a supernova environment. The r process probably occurs in the envelopes of type II supernovae when the high ion temperature precursor of the shock wave becomes strong enough to cause helium spallation, with copious neutron formation and ultimate production of deuterium⁵⁻⁷. The presupernovae of type II seem to be stars of at least $4 M_{\odot}$. In the following discussion I shall assume that the s-process products are uniformly distributed in space; to the extent that this may not be true, the effects discussed will be amplified.

Reeves⁸ has recently applied the analysis of Spitzer⁹, of the slowing down of supernova debris through interaction with the interstellar medium, to a discussion of the thoroughness of the mixing of the supernova products throughout the interstellar medium. A type II supernova will probably interact dynamically with about $10^4 M_{\odot}$ of gas in slowing down in about 10^6 yr. Reeves assumes that the supernova nucleosynthesis products are intimately mixed with this material, and that mixing with additional material will continue during the course of a few more million years as a result of random motions of the gas. On this basis he concludes that any typical part of the gas will be contaminated with fresh supernova debris every few million years, and that the isotopic composition of the interstellar medium will be maintained the same over a large local volume of the Galaxy.

This analysis does not, however, take into account the effects of the interstellar magnetic field. Even in typical neutral hydrogen clouds the magnetic field is effectively tied to the gas because of ions produced by ultraviolet radiation. Some mixing of supernova debris across field lines may take place as a result of short-scale dissipation processes, particularly during the early part of the supernova envelope expansion. A typical type II supernova explosion is likely to eject only a few solar masses of material, and this may perhaps be mixed into only about $10^2 M_{\odot}$ of the $10^4 M_{\odot}$ which participate in the dynamics of the slowing down process. Because of the operation of Rayleigh-Taylor instabilities, the supernova debris is likely to end up in the form of many thin tubes of magnetic flux threading through the much larger amount of material which has participated in the dynamical deceleration. Subsequent mixing would be mainly confined to longitudinal diffusion along the field lines, a very slow process.

There are about $10^{10} M_{\odot}$ of gas in the Galaxy, and about one type II supernova explosion per 10^2 yr. Thus it may be that any given part of the interstellar medium has received a direct injection of the debris from only about one of these supernovae.

Processes do, however, exist which should ultimately lead to complete mixing of material. Material in very dense interstellar clouds is shielded from ultraviolet light, so that significant drifting across field lines may occur, particularly for elements with higher ionization thresholds. Under these circumstances, heavier atoms can also adhere to interstellar grains, which can drift across field lines more easily than ions. Occasionally interstellar material will participate in a star formation event, in which $\sim 10^4 M_{\odot}$ collapse to high density with fragmentation to form stars in what become expanding associations. The condition that a newly-formed association of stars should be unbound is that more than half of the collapsed mass should be ejected, presumably as gas which never

became part of the stars. Since the interstellar magnetic field can slip out of the collapsing gas¹⁰ when the density exceeds 10^6 atoms cm^{-3} and since the collapsing gas is likely to be turbulent, thorough mixing will occur at that time. Truran and Cameron¹¹ have estimated that about half the interstellar medium had been through stellar interiors at the time of formation of the Solar System. From these various considerations I estimate that the products of stellar nucleosynthesis probably become homogenised in the interstellar medium after about 3×10^9 yr, but that more recent products remain localised in thin tubes of magnetic flux.

Although it seems that the production of the more abundant lighter elements was concentrated toward the early history of the Galaxy, the s and r processes are of secondary and tertiary character, transforming previous products of nucleosynthesis. Thus for the present purposes it is sufficient to suppose that the heavy elements have had a uniform production rate throughout galactic history. Thus at the time of formation of the Solar System, the interstellar cloud complex which was about to collapse probably had about 80% of the heavy elements uniformly distributed throughout the mass, on which was superposed a highly local fluctuation in abundance of the order of 25% of the average abundance.

During the collapse, turbulent mixing would tend to reduce these local fluctuations¹². After fragmentation, the gas would settle into differentially rotating flattened gaseous disks, which would then dissipate to form stars. Differential rotation would tend to homogenise composition at any given radius, but some small radial composition differences might persist. This might be the source of the strontium isotopic differences characteristic of BABI and ADOR, and the related lead-lead differences. In the following I assume that there was a fractional difference of Δ in the r-process abundances in BABI and ADOR, and enquire what effects this would have on strontium and uranium isotopic abundances.

The strontium case is actually very complicated. ^{86}Sr and ^{87}Sr are s-process isotopes, except for the small leakage of the r process to the latter through ^{87}Rb , which has a half-life four times the age of the Galaxy. Because mass spectrometers sometimes suffer from mass fractionation problems in the ion source, however, the common practice is to refer the abundance of ^{87}Sr to the slope of abundances between ^{86}Sr and ^{88}Sr . The latter isotope has both s and r-process components. Furthermore, the s-process neutron capture path passes through ^{85}Kr , which has a half-life of 10.76 yr. A recent analysis by Scalo and Ulrich⁴ indicates that the s process may occur in a series of relatively short neutron bursts. So the s-process path probably divides at ^{85}Kr , producing both ^{86}Sr and ^{86}Kr . By itself, this may introduce some fluctuations in the $^{87}\text{Sr}/^{86}\text{Sr}$ ratio, but I shall ignore this complication here. One cannot, however, take the abundance of ^{86}Kr as indicative of the local r-process abundance.

The other neighbouring r-process-only isobars are ^{82}Se , ^{96}Zr and ^{100}Mo , with abundances of 6.18, 0.784 and 0.385, respectively, on an abundance scale¹³ where silicon = 10^6 . An interpolation suggests the r-process abundance contribution to ^{88}Sr to be about 2.5 out of a total abundance of 22.2. A fractional abundance fluctuation Δ in this contribution would thus produce a fluctuation $0.5 (2.5/22.2) \Delta = 0.056 \Delta$ in the $^{87}\text{Sr}/^{86}\text{Sr}$ ratio that would be inferred from analysis of mass spectrometer measurements. The fractional difference between BABI and ADOR of 2.0×10^{-4} would thus imply $\Delta \approx 3.5 \times 10^{-3}$. This estimate must be regarded as uncertain by a factor three. Nevertheless the fluctuation represents a reduction by two orders of magnitude from the local fluctuations that may have characterised that part of the interstellar medium which collapsed to form the Solar System.

The analysis of the uranium isotopes must be even cruder because of their radioactive character. The fractional abundance of a radioactive isotope, relative to the total amount ever formed, is the ratio of its mean life to the total time needed to accumulate a non-radioactive nuclide at the recent production

rate. The mean life of ^{238}U is 6.4×10^9 yr, or twice the time required for homogenisation of abundances. The homogenised background of this nuclide may thus be about 50% of the total, with local fluctuations in abundance of the order of a factor two. The mean life of ^{235}U is 1.02×10^9 yr. The homogenised background abundance level is thus only about 4% of the average, and local fluctuations may be an order of magnitude about the mean. There will be some correlations between the abundance fluctuations of ^{235}U and ^{238}U . I estimate the fluctuations that may occur in the radiogenic $^{207}\text{Pb}/^{206}\text{Pb}$ ratio to be of order 20Δ , but not even the sign of these can be predicted, because a region with excess r-process production might or might not have had a recent contribution within the homogenisation time, and thus the ^{235}U might be high or low when there is an r-process excess.

For what it is worth, the difference in $^{207}\text{Pb}/^{206}\text{Pb}$ ratios between Angra dos Reis and the other two basaltic achondrites implies an order of magnitude $\Delta \sim 0.019/20 \sim 10^{-3}$. Since in this case it seems that ^{235}U is in excess in Angra dos Reis, it is perhaps not surprising that this meteorite also has a large component of the fission decay products of ^{244}Pu , an extinct radioactivity with a half-life of 82×10^6 yr (ref. 14).

Thus it seems that a case can be made that the isotopic differences between Angra dos Reis and other basaltic achondrites may be due to real fluctuations between the relative abundances of s-process and r-process nucleosynthesis products at a level $\Delta \sim 10^{-3}$. These differences are at a level which is subject to detection by careful mass spectrometry. The optimum ranges of elements in which to seek such effects are those in which there are comparable abundances from the two processes. Elements of even atomic number in the range from germanium to tellurium are probably most suitable for these measurements. If such differences should be found, this would provide a new tool for finding difference source regions in which Solar System materials have accumulated.

After this letter was submitted, I learned of the important work of R. N. Clayton, L. Grossman, and T. K. Mayeda (personal communication) showing that individual minerals in carbonaceous chondrites contain variations in oxygen isotope ratios that must represent different mixtures of separate nucleosynthetic processes. The general theoretical considerations given here should also provide an explanation of these effects.

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Post-depositional Remanent Magnetisation in Deep-sea Sediment

SEDIMENTS of various lithologies cored from most parts of the deep ocean floor have been found to contain a record of the past behaviour of the Earth's magnetic field, especially the sequence of reversals over at least the past 5 m.y. (ref. 1). The mechanism by which these sediments acquired their natural remanent magnetism (NRM) is, however, still poorly understood. We have recently conducted experiments that indicate that post-depositional remanent magnetisation² is a viable mechanism of magnetisation of deep-sea sediments.

Laboratory studies of the most obvious mechanism, depositional or detrital remanent magnetism (DRM), have shown that the remanent inclination is usually shallower than the field inclination in which the sediment was deposited^{3,4}. The difference is thought to be due to the effects of gravity overcoming magnetic-orienting couples of the magnetised grains at the instant of deposition⁵. The NRM inclinations of deep-sea sediments generally agree, however, with the expected axial dipole field inclinations⁶. It has been suggested⁷ that these sediments may acquire their remanent magnetism shortly after deposition, by the post-depositional mechanism observed in synthetic sediment². The physical origin of this remanence is likely to be closely related to Brownian motion⁸. In deep-sea sediments, a remanence may be acquired as a result of sediment disturbance by benthic organisms⁹. The natural remanent magnetism of some sediment may also be of chemical origin as a result of *in situ* authigenic growth of ferromagnetic minerals¹⁰.

Deep-sea sediment was obtained from the bottom of a Lamont core, RC14-14, the magnetic properties of which have been reported¹¹. The NRM was of a stable type; alternating fields necessary to randomise 50% of the original NRM (median destructive fields) averaged 200 oersted. The average magnetic inclination of the core was not significantly different from the axial dipole field inclination at the core site. The dominant magnetic minerals were essentially magnetite and titanomagnetite (compositional parameter, $x=0.53$) which were incorporated in a matrix of diatomaceous clay.

A quantity of the sediment was thoroughly dispersed in a sufficient amount of distilled water to form a thick slurry,

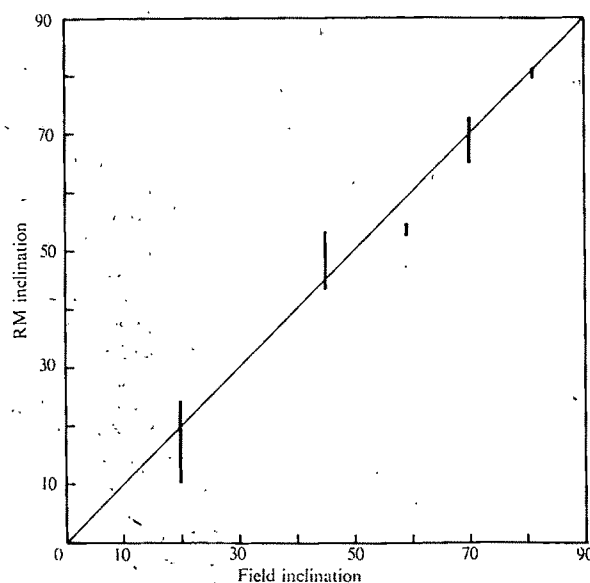


Fig. 1 Inclinations of the control field and the remanent magnetisation of the reconstituted sediment. Error bars represent range of remanent inclinations for each sample; the line of perfect agreement is shown. Successively steeper inclinations were produced in fields of 0.20, 0.28, 0.38, 0.59 and 1.20 oersted, respectively.

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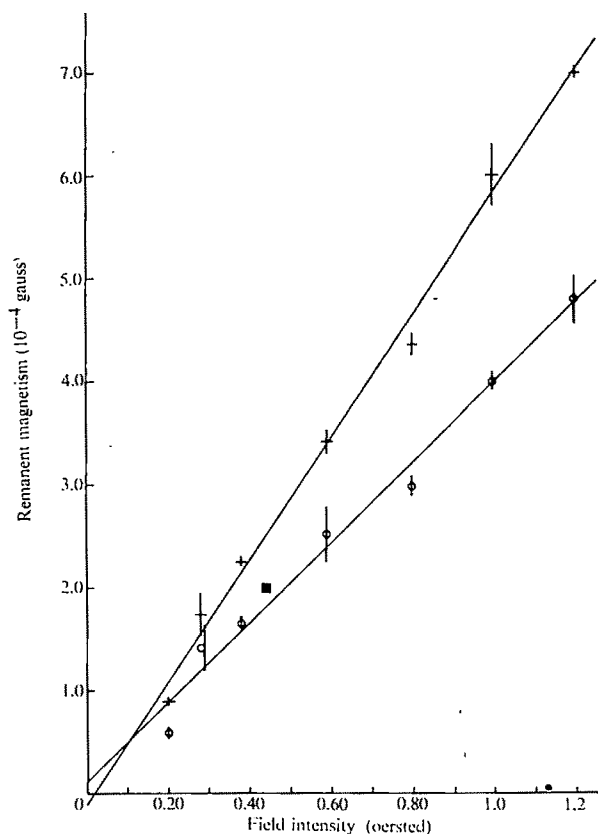


Fig. 2 Intensities of the control field and the remanences of the reconstituted sediment, before (+) and after (Φ) 100 oersted a.f. demagnetisation. Regression line slopes are 5.96 ± 0.19 ($\times 10^{-4}$ gauss oersted $^{-1}$) and 3.87 ± 0.20 ($\times 10^{-4}$ gauss oersted $^{-1}$), respectively. ■, Average remanent intensity of RC14-14, after 100 oersted a.f. demagnetisation¹¹, plotted against the present axial dipole field intensity at the core site.

similar in consistency to that normally found near the tops of piston cores immediately after coring. The sediment slurry was spooned into plastic cylinders (diameter 7 cm, height 5 cm) that had perforated bottoms covered with paper towelling to prevent sediment loss. Helmholtz coils were used to provide various field intensities and directions. The sediment slurry was thoroughly stirred in the presence of a known field and allowed to dry in this same field. Two or three specimens were cored from each sample with a plastic cylinder after the sediment became cohesive yet not completely dry (generally after 4 to 7 d). The remanent magnetism of each specimen and that remaining after partial alternating field (a.f.) demagnetisation¹² were measured with a slow-spin magnetometer. Unreliable results were obtained if the sediment was too wet.

The remanent inclinations agreed reasonably well with the inclinations of the control fields (Fig. 1). No systematic deviation of the remanent magnetism direction from that of the control field, such as inclination error^{4,13}, was observed. The scatter of directions among specimens from an individual sample is attributed chiefly to specimen orientation errors and, more important, to visible deformation of the sediment resulting from partial desiccation.

The remanent intensity was linearly proportional to the intensity of the control field, at least up to 1.2 oersted (Fig. 2). The regression line through either the remanent intensities or the partially demagnetised remanences intersects the ordinate at a value not significantly different from zero magnetisation intensity. Only 35% of the remanence was randomised by 100 oersted a.f. demagnetisation as illustrated by the different slopes of the two lines. Alternating field demagnetisation curves of individual specimens show median destructive fields of about

200 oersted, with corresponding directional changes of less than 10° .

The process of stirring the sediment in the presence of a magnetic field may be analogous to the activities of benthic organisms at, or just beneath, the sediment-water interface on the ocean floor¹⁴. Core RC14-14 shows evidence of benthic organism activity or bioturbation over most of its length¹¹. The NRM of the core and the remanence of the reconstituted sediment are similar in intensity (Fig. 2), in stability against alternating fields and in their apparent lack of systematic inclination error. This evidence suggests that the stable NRM is a post-depositional remanent magnetisation acquired in conjunction with physical disturbance by benthic organisms in most sections of the core.

Mixing of deep-sea sediment by benthic organisms is seen from photographs to be a common feature of the ocean bottom environment¹⁵ and evidence of it is found in many sediment cores^{16,17}, which often contain good magnetic records^{18,19}. Therefore, a substantial portion of deep-sea sediment may have acquired an NRM as a result of a sediment-mixing process. This is not to say that mixing is a prerequisite for the acquisition of post-depositional remanence in sediment. Preliminary results show that the same sediment acquires a stable remanence in the direction of an applied field without stirring. It has no inclination error but has a somewhat lower intensity. Even if the DRM mechanism is also a factor in the original magnetisation of deep-sea sediment, realignment of this type of remanence may occur after deposition. The small grain diameters of magnetic minerals often encountered in deep-sea sediment (generally $40\% < 1 \mu\text{m}$)²⁰, coupled with the field dependence and lack of inclination error of this post-depositional remanence, support the Brownian motion model of magnetic grain alignment in a field in the sediment^{8,21}.

The extent to which the sediment and its observed remanent magnetism are contemporaneous must vary with depth of faunal activity and other factors controlling the immobilisation of magnetic grains in the sediment. These include grain size, grain magnetic moment and sediment-water content. The mean burrowing depths are apparently only about 5 cm in deep-sea sediment, although some burrows can infrequently extend deeper^{17,22,23}. Preliminary laboratory observations indicate that only a small decrease in water content is necessary to lock-in a post-depositional remanence in the sediment. This suggests that the difference in depth between acquisition of remanence and the sedimentation surface may not be excessive.

The applicability of such sediment reconstitution studies to palaeofield intensity measurements in deep-sea sediments is now being investigated.

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Flocculation of Latices by Low Molecular Weight Polymers

POLYELECTROLYTES are increasingly being used as flocculants for electrostatically stabilised dispersions of colloidal particles in such diverse fields as water treatment and mineral processing¹. Suitable polyelectrolytes, which are usually effective at low concentrations (≤ 10 p.p.m.), invariably have a high molecular weight² (a viscosity average molecular weight $M_v > 10^5$). They seem to function by a bridging mechanism whereby the flocculant interferes with the free movement of the particles¹⁻⁶.

We now report that even low molecular weight non-ionic polymer molecules ($M_v \geq 10^3$ to 10^6) are able to flocculate some polymer latices. They also seem to function by a bridging mechanism but require the presence at the particle surfaces of suitable groups with which the flocculant can interact specifically.

The new phenomenon was first discovered with an apparently electrostatically stabilised aqueous polystyrene latex (mean radius 24 nm), prepared by the method of Ottewill and Shaw⁷. Figure 1a displays the course of flocculation, which was followed turbidimetrically, on addition of poly(ethylene oxide) (PEO) to the latex at 35°C. (The initial light scattering was compensated for.) Several samples of low molecular weight PEO (ex Union Carbide Australia Ltd) were examined using the latex at a particle concentration of $\sim 10^{12}$ cm⁻³. In the absence of PEO the particles exhibited long term stability, whether or not 0.2 M HCl was present (line 1). When low molecular weight PEO was added in the absence of 0.2 M HCl no flocculation could be detected at any polymer concentration. But the addition of PEO, at 20 p.p.m., of either $M_v = 4,000$ or 23,000 in the presence of 0.2 M HCl resulted in rapid flocculation of the latex (curves 2 and 3). The higher molecular weight polymer was the more effective. Very high molecular weight polymer $M_v = 1 \times 10^6$ was also an effective flocculant at concentrations of only a few p.p.m.

Polystyrene latices prepared by the method of Ottewill and Shaw⁷ possess surface carboxylic acid groups^{8,9}. To investigate the role of these groups, polystyrene latices were prepared at low temperatures ($< 30^\circ$ C); as we have shown elsewhere¹⁰, such latices possess no detectable surface carboxylic acid groups. Interestingly these latices failed to flocculate on addition of PEO in the presence of 0.2 M HCl. On the other hand, polystyrene latices sterically stabilised¹¹ by poly(acrylic acid) (PAA) of $M_v = 19,300$ were also found to be flocculated by low (and high) molecular weight PEO (Fig. 1b). Again 0.2 M HCl was necessary for flocculation. We note that in the absence of PEO these latices exhibit long term entropic stabilisation¹¹ (line 4).

The foregoing experiments point to the central role played

by the surface carboxylic acid group in promoting flocculation. They suggest the following mechanism for flocculation by low molecular weight polymers: At suitably low pH the surface carboxylic acid groups are predominantly unionised and so can H bond with the ether oxygens of the PEO chains. The occurrence of such H bonding is forcefully demonstrated by the phase separation of mixtures of PAA and PEO from aqueous solutions at low pH (refs 12 and 13). For the conditions relevant to curve 3 in Fig. 1a, the centres of the particles were separated, on average, by $\sim 1,000$ nm, if a cubic array is assumed. The r.m.s. end-to-end length of the PEO chains was calculated¹⁴ to be only ~ 10 nm. Obviously on average the polymer chains could not possibly span the distance between the particle surfaces. Therefore the PEO chains may reasonably be inferred to have become attached to one particle by H bonding to the surface carboxylic acid groups and to have become attached to a second (or more) particle(s) in subsequent Brownian collisions. Free movement of the latex particles was thus prevented, corresponding to bridging flocculation. According to this postulated mechanism, no flocculation would be expected at higher pH values because the ionised carboxylic acid groups would be unable to H bond with the PEO. Also no flocculation would be expected in the absence of surface carboxylic acid groups. Both expectations were realised.

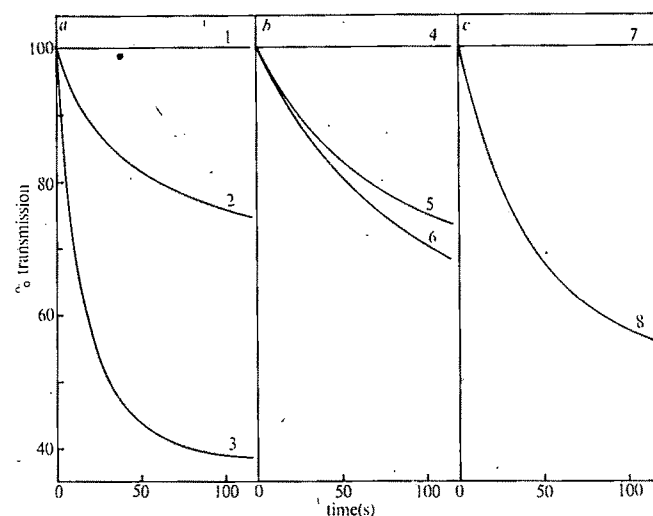


Fig. 1 The % transmission as a function of time for polystyrene latices. *a*, Curves for latices containing surface carboxylic acid groups: 1, no PEO added; 2, PEO of $M_v = 4,000$ added; 3, PEO of $M_v = 23,000$ added. *b*, Curves for latices stabilised by PAA: 4, no PEO added; 5, PEO of $M_v = 4,000$ added; 6, PEO of $M_v = 23,000$ added. *c*, Curves for latices stabilised by PEO: 7, no PAA added; 8, PAA of $M_v = 19,300$ added. Flocculant added at 20 p.p.m. in *a* and *c* and 50 p.p.m. in *b*.

If this explanation is correct then it is also predicted that low molecular weight PAA should be able to flocculate latices stabilised solely by PEO chains. Figure 1c shows the flocculation induced by the addition of PAA ($M_v = 19,300$) to a polystyrene latex sterically stabilised in this case enthalpically by PEO ($M_v = 23,000$). Again no flocculation was evident unless 0.1 M HCl was also present to convert most of the carboxylic acid groups into the unionised form.

The phenomenon seems to be closely analogous to the bridging flocculation observed with high molecular weight polyelectrolytes. Both are characterised by the intervention of the polymeric flocculant by promoting 'sticky' collisions between the particles, the flocculated particles often being separated by some distance¹⁵. There is thus no need to reduce to near zero the repulsive potential energy between

the particles, whether electrostatically or sterically generated, to permit flocculation to occur.

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BIOLOGICAL SCIENCES

Genetic Differences in Conformational Changes of Albumin in the House Mouse

THE ability of mouse liver to convert mouse or bovine albumin to a faster migrating band under acid conditions of electrophoresis has recently been found to be controlled by a dominant gene, as observed in the SWR/J and several other strains of mice¹. Other strains, such as C3H/HeJ, had the recessive allele and were unable to convert albumin. The conditions used included a pH at which conformational changes in albumin are known to occur, suggesting that the strains of mice differ in a factor in the liver capable of converting albumin to a different conformational state. I report here evidence that the conversion of albumin can be reversed by lowering the pH markedly. This provides further evidence that a conformational change has taken place.

Livers from male C3H/HeJ and SWR/J mice were homogenized and centrifuged, and the supernatant was extracted using procedures described before¹. One volume of horse serum albumin (HSA, Fraction V, Sigma, 5 mg ml⁻¹ in 0.25 M sucrose) was added to 9 volumes of extract. An equal volume of solvent (citric acid, monohydrate: 15% sucrose, 1:5 (w/v), plus 6 M urea) was added to each extracted sample. Before electrophoresis 10 μ l was added to a slot, 5 volumes of an aliquot was diluted with 1 volume of concentrated HCl and 20 min later 12 μ l was added to another slot, and finally 10 μ l of an aliquot untreated with HCl was added to a third slot. Controls were also included in which 0.25 M sucrose replaced HSA or liver supernatant, but were otherwise handled as other

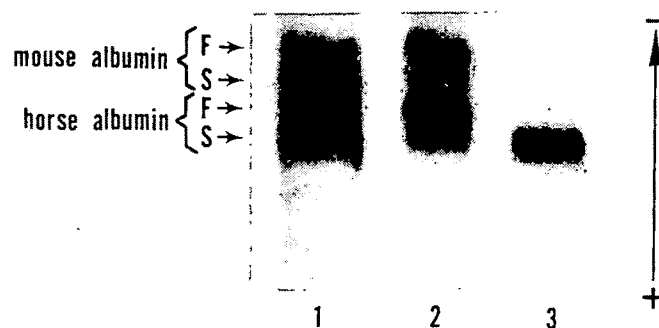


Fig. 1 Electrophoretograms showing the effect of liver extract and HCl on HSA. Channels 1-3 are (1) HSA+SWR/J liver extract+HCl; (2) HSA+SWR/J liver extract, and (3) HSA. Electrophoresis was as previously described¹. Gel buffer was 0.05 M Tris-citric acid, pH 2.4+3 M urea+10% 'Cyanogum'-41. Electrode buffer was 0.2 M glycine-citric acid, pH 3.5.

samples, although not treated with HCl. HSA was used because both slow and fast forms were electrophoretically distinct from proteins of mouse liver.

Results are shown in Fig. 1. HSA was present as a single, slower migrating band when not combined with liver (channel 3), whereas most was converted to a faster band when combined with liver extract of the SWR/J strain (channel 2). The latter result was not affected by the time when the sample was added to the slot, that is, before addition of HCl to an aliquot more than 20 min before electrophoresis compared with just before electrophoresis. Treatment with HCl (channel 1) lowered pH markedly (from 2.83 to 0.05) and converted much of the HSA to the slower migrating band. In C3H/HeJ mice (results not shown) HSA was not converted to a faster migrating band, but consisted only of a slow band migrating the same distance as in channel 3, with or without added HCl. Most of the mouse albumin of liver was also converted to a faster migrating band in the SWR/J but not the C3H/HeJ strain, as described previously¹; treatment with HCl converted a large portion to the slower migrating band in the SWR/J strain (Fig. 1), but there was no change in the C3H/HeJ strain.

My data show that liver of one strain of mouse but not of another can convert HSA to a faster migrating form. The genetic difference is clearly not in the primary structure of albumin, that is, amino acid sequence, since the same source of HSA was used in all preparations, but is rather a secondary alteration of the molecule. A conversion to a different conformational state is highly likely in view of the reversal from the faster to the slower migrating band after treatment with excess acid, especially since lowering the pH below 3.5 favours the expanded, slower migrating form². The reversibility of the change in albumin renders untenable the hypothesis that conversion of albumin from a slower to faster migrating form results from cleavage of a portion of the albumin molecule. These results point to the existence of two genes which control the structure of albumin, that is a conventional "structural gene" specifying primary structure³ and a second gene affecting secondary or tertiary structure.

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Platelet Contractile Regulation in an Isometric System

We have previously shown that human platelets, in addition to actomyosin, the so-called thrombosthenin¹, contain a tropomyosin-like protein². Furthermore, we provided evidence for the presence in isolated platelet actomyosin of a control system which "turns-on" the Mg-ATPase of the contractile protein complex at a saturating level of 10^{-6} M Ca^{2+} (ref. 2).

Platelet contraction has usually been considered to be an irreversible process. Platelets have been found, however, to contain a membrane-associated relaxing factor, resembling the muscle sarcotubular system. This factor sequesters calcium from solution and behaves as a Ca^{2+} pump^{3,4}. It has been shown recently that in an isotonic contractile system, a platelet-containing clot relaxes in the presence of papaverine, theophylline or cytochalasin B (ref. 5). Here we used an isometric system to measure platelet contraction and relaxation and the calcium-sensitivity of these processes.

Cylindrical clots were obtained by pouring a human platelet-rich plasma suspension, immediately after thrombin addition, into siliconized glass tubes, 6×0.6 cm internal diameter, plugged at one end with parafilm. Saline was carefully layered over the suspension to abolish the meniscus. After 10 min the clot cylinder was poured into a Petri dish containing ice cold Tyrode solution to inhibit contraction. The clot was then tied at one end with a cotton thread to a rigid glass support and at the other end to a Grass force displacement transducer (FT 03 C) linked to a Grass Polygraph d.c. driver amplifier recording system. The clot was immersed in a bath of Tyrode solution containing 1.7 mM Ca^{2+} at 37°C and the tension was recorded.

The tension developed in the clot in this Ca^{2+} -containing isometric system increased with rising platelet concentration, similar to observations on clot retraction measured in a contractile isotonic system^{6,7}. The maximal tension was proportional to the initial cross-sectional area of the clot, and was independent of its length. Unlike in a muscle system, the cross-sectional area of the clot greatly decreased during isometric contraction, presumably as a result of transverse contraction associated with extrusion of serum from the fibrin-platelet network. In the Ca^{2+} -containing isometric system (experimental conditions described in the legend to Fig. 1), platelet-rich clots developed tension at an initial speed of $0.2 \text{ mg min}^{-1} \text{ cm}^{-2}$ (initial cross-sectional area) and reached a maximal tension of 1.8 mg cm^{-2} after 15 min. After maintaining a tension plateau for about 5 min, the clot relaxed spontaneously and irreversibly at a rate approximately half that of the development of the tension. This spontaneous irreversible

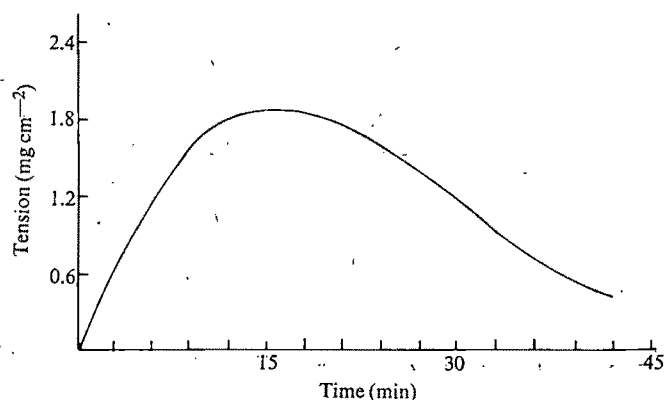


Fig. 1 Tension development in thrombin-clotted platelet-rich plasma in a Ca^{2+} -containing isometric system. Citrated platelet-rich plasma, 2 ml, containing $300,000 \text{ platelets mm}^{-3}$ and 250 mg% fibrinogen, were clotted with 0.5 NIH units thrombin (Parke-Davis). The clot was incubated at 37°C in Tyrode solution, containing 1.7 mM Ca^{2+} . The tension recorded is expressed in mg cm^{-2} (initial cross-sectional area).

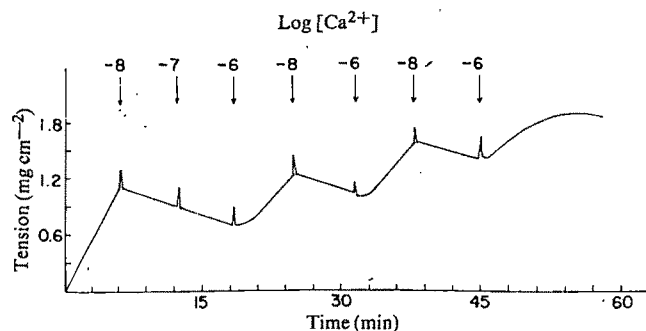


Fig. 2 Effect of Ca^{2+} on the tension developed in a thrombin-clotted platelet-rich plasma. Except for Ca^{2+} concentration, the conditions were the same as in Fig. 1. The clot was washed and incubated in Tyrode solution containing variable Ca^{2+} concentrations in the pre-maximal contraction phase. Appropriate mixtures of 10 mM EGTA and 10 mM Ca-EGTA were used to obtain the desired Ca^{2+} concentrations, taking into account a dissociation constant of 1.9×10^{-7} for Ca-EGTA (ref. 29).

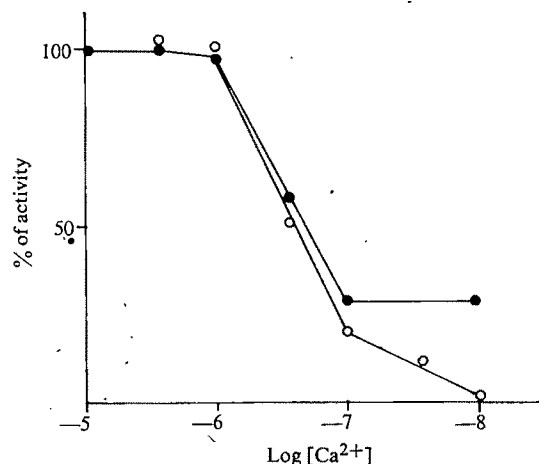


Fig. 3 Effect of Ca^{2+} on isotonic clot retraction and on Mg-ATPase activity of human platelet actomyosin. O, Citrated platelet-rich plasma was clotted with 0.5 NIH units ml^{-1} of thrombin in flamed test tubes in the presence of 10^{-8} M to 10^{-5} M Ca^{2+} adjusted with Ca-EGTA buffer as in Fig. 2. The percentage of clot retraction was calculated from the measured volume of expressed serum, 100% being defined as maximal clot retraction. ●, Mg-ATPase activity of human platelet actomyosin at varying Ca^{2+} concentrations was estimated as described elsewhere².

relaxation may be a sequel to platelet ATP depletion known to occur as a result of thrombin action^{8,9} and possibly to platelet membrane damage inherent in viscous metamorphosis¹⁰.

When a contracting clot, at pre-maximal tension, was treated with Ca^{2+} -free Tyrode solution containing 0.05 M ethylene glycol-bis-(2-aminoethyl ether) N,N'-tetraacetic acid (EGTA, a selective Ca^{2+} -chelator), relaxation immediately occurred (Fig. 2). When subsequently bathed again in Ca^{2+} -containing Tyrode, the clot contracted at the original initial speed. Addition of EGTA at the time when maximal tension was reached or later did not affect the speed of the spontaneous relaxation. When a contracting clot had developed half its maximal tension, it could be relaxed by lowering the free Ca^{2+} concentration (by the use of an EGTA-Ca buffer) to 10^{-8} M. The minimal concentration of Ca^{2+} required for maximal contraction was found to be 10^{-6} M, similar to muscle and platelet natural actomyosin systems². Cycles of contraction and relaxation could be induced several times in the same clot by varying the Ca^{2+} concentration (Fig. 2).

The effect of Ca^{2+} in a standard isotonic clot retraction system was studied for comparison. Retraction of a thrombin-treated platelet-rich plasma clot was half maximum at 3×10^{-7} M Ca^{2+} and reached maximum value above 10^{-6} M Ca^{2+} (Fig. 3). The latter Ca^{2+} concentration was identical

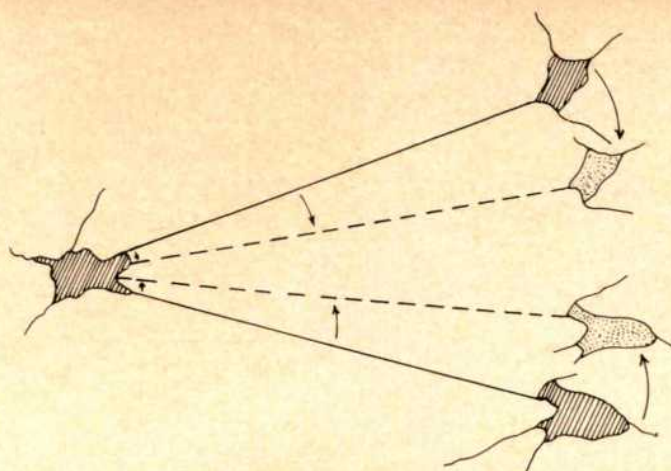


Fig. 4 Clot concentration model. Platelet masses connected by fibrin fibres. The contraction of the platelet masses results in a reduction of the angle between the fibrin fibres. —, Fibrin fibre before contraction; ---, fibrin fibre after contraction.

to both that required for maximal ATPase activity of thrombosthenin and that required for maximal tension of the platelet-rich plasma clot in the isometric system described here.

This study has shown that the clot contraction-relaxation cycle depends upon the presence of Ca^{2+} . Calcium, particularly intracellular platelet calcium, has long been suspected to be an essential requirement for clot contraction⁷. Indeed, platelets have been shown to contain high concentrations of Ca^{2+} which could be released by thrombin¹¹. The presumably intracellularly-bound Ca^{2+} would, in the process of release, be expected to interact with specific platelet actomyosin sites^{12,13}; subsequent interaction between actin and myosin would then occur and contraction would follow. In our study, thrombin-treated platelets showed permeability properties similar to glycerinated or skinned muscle fibres rather than intact muscle fibres, as they responded to externally added EGTA.

Two mechanisms may be suggested to account for the dependence of platelet contraction on the exterior concentration of EGTA-Ca^{2+} : the action of Ca^{2+} on thrombosthenin located on the outer surface of the platelet membrane, or the occurrence of a selective change in the platelet membrane permeability. In support of the first mechanism several authors have found thrombosthenin and thrombosthenin-specific ecto-ATPase on the external surface of the platelet membrane¹⁴⁻¹⁷, but these studies are considered inconclusive¹⁸. In support of the second mechanism it may be mentioned that thrombin is able to hydrolyse platelet membrane proteins¹⁹⁻²¹. Consequently, a change of platelet membrane protein conformation might occur and affect the local lipid structure, as has been discussed by Singer^{22,23} for hypothetical models. In addition, extracellular calcium can bind to phospholipid heads of synthetic lipid bilayers, neutralize their charges and produce a compression wave which is effective at long distances²³⁻²⁵. Such Ca^{2+} -generated compression waves might cause structural changes in proteins embedded in these lipid bilayers²³. This effect may explain the need for extracellular Ca^{2+} for platelet aggregation and contractile processes. Furthermore, thrombin has been shown to increase the rate of Ca^{2+} uptake by platelets¹¹.

The generation of tension in a contracting clot involves two processes, platelet contraction itself, and fibrin network collapse with extrusion of trapped serum. The mechanism by which platelets pull the fibrin fibres together is poorly understood. We venture to propose a model (I. C., and E. Katchalski, unpublished) taking into account the rigidity of the fibrin fibres which during clotting become intimately associated with the platelet membranes and converge towards the platelet

masses^{26,27}. Contraction of the platelet mass would reduce the angle between the attached fibrin fibres, their approximation amplifying with distance. Other platelet masses associated with these fibrin fibres would approach each other and tension would be generated in the clot (Fig. 4).

The clot contraction-relaxation cycles demonstrated in our experiments stress the physiological significance in platelets of both the sarcotubular system, functioning as a Ca^{2+} pump, and the contractile protein regulatory system. Our previous observations²⁸ support a regulation of the platelet contractile process of an actin-linked tropomyosin-troponin type rather than of a myosin-linked type.

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Does Gonadotrophin-induced Ovulation in Mice cause Malformations in the Offspring?

GONADOTROPHIN treatment affects follicular maturation and induces ovulation in immature and mature mammalian females. This procedure has been used for experimental

research¹⁻⁸ as well as for clinical treatment in human anovulatory disease. Side effects reported when hormonally induced ovulation is followed by pregnancy include: frequent resorptions, spontaneous abortions with chromosomal anomalies, extrauterine and multiple pregnancies and difficulties in giving birth⁹⁻¹⁶.

This article demonstrates that after hormonally induced ovulation, malformations can occur in the embryos of mice. This is of interest, as Dyson and Kohler reported two clinical cases of anencephaly following gonadotrophin-induced ovulation¹⁷.

Ninety randomly bred virgin mice (Swiss albino), 6 to 9 weeks old, were caused to ovulate by intraperitoneal injections of 5 IU pregnant mare's serum gonadotrophin (PMS, 'Gestyl', Organon, Holland) in 0.15 ml of 0.9% saline and of 5 IU human chorionic gonadotrophin (HCG, 'Pregnyl', Organon, Holland) in 0.1 ml of 0.9% saline 48 h later. After the second injection the females were caged overnight with males (same strain and of proven fertility). Insemination was verified the following morning by the presence of a copulatory plug.

Table 1 Observations on Pregnant Females Following Gonadotrophin Treatment and Normal Mating

	Number	Injected (%)
Treated	90	
Mated	36	38.9
Pregnant	32	34.4
		Pregnant (%)
Deaths*	2	6.5
Normal delivery†	2	6.5
Complicated delivery‡	2	6.5
Blocked delivery§	26	80.6

* Death after hormone treatment occurred on the 18th d of gestation. These females had three and twelve normal foetuses respectively.

† One female gave birth to thirteen normal embryos, the other delivered three living and eight dead embryos.

‡ Females which had difficulties during delivery started to give birth to both dead and living embryos. They also failed to give complete birth, feeding on the embryos delivered first. They were autopsied 6 h after they had started to deliver; the normal length of the delivery procedure does not exceed 2 h. Living foetuses were still found in the uterus.

§ Untreated control females delivered between the 19th and 20th d of gestation, so animals which had shown blood-stained vaginal smears for 2 d were killed between the 19th and 21st d, the uteri were opened and respiration was induced manually in the individual embryos. Those which survived more than 1 h were placed with foster mothers, which had delivered on the same day and had been deprived of their litters.

Table 2 Reproductive Performance of Gonadotrophin-treated Females

	Treated	Control
Litters	32	8
Litters with anomalies	5	0 0.05 > P > 0.01
Average litter size	14.3 ± 6.5	12.4 ± 2.7*
No. of nidations	665	112
Living offspring	48.5%	93.8%
Dead foetuses	20.3%	1.8%
Anomalous (total offspring)	1.8%	0 0.01 > P > 0.001
Resorbed in utero	31.2%†	4.5%
No. of sexed embryos	336	521‡
Males	35.5%	51%
		P < 0.001
Females	64.6%	49%
Embryos placed to foster mothers	184	84
Viability up to 1 h	76%	99%
Survival to 23 d	66%	85%

* In addition to the controls (Caesarean sectioned), twenty-four normally delivering females of the same strain were used to estimate average litter size.

† Partly with malformations.

‡ For the estimation of the sex ratio in controls, an additional thirty-six normally delivering females of the same strain were used.

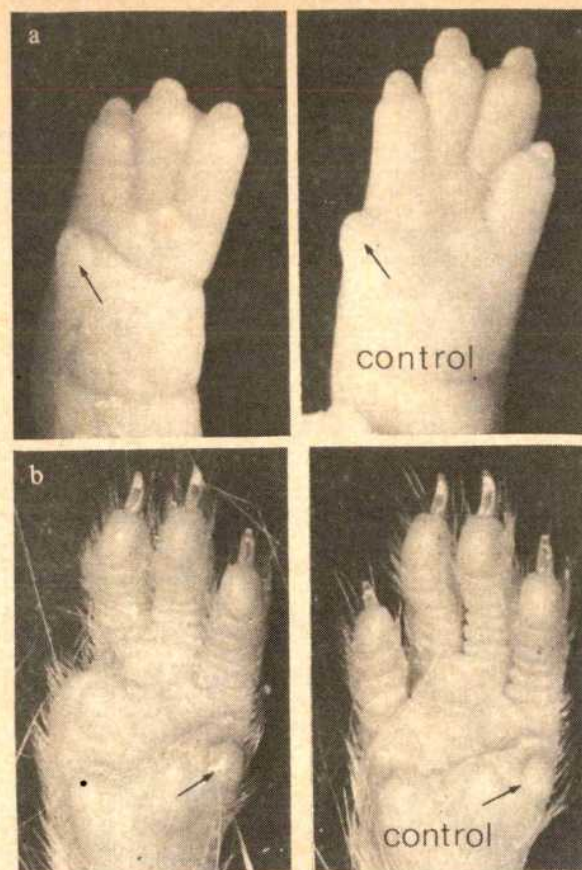


Fig. 1 Malformations of the forepaw (aplasia of the 5th digit, thumb arrowed). *a*, Left forepaw of newborn mice; *b*, right forepaw of mice 23 d post partum (the offspring of the treated female died at this age).

This day was designated as day 1 of pregnancy. No further treatment was given.

The results obtained with gonadotrophin-treated and normally mated mice are given in Table 1. Details of pregnancies at the time of autopsy of females subjected to gonadotrophin treatment are given in Table 2. The litters of females injected with hormones ranged in size from two to twenty-six, control litter size was between nine and sixteen. Although 99% of a total of eighty-four control embryos could be placed to foster mothers, only 76% of the embryos (total 184) obtained from treated females survived the first hour. Most of the embryos of injected females died within the first 5 d and those which lived to 23 d post partum survived thereafter. Death of controls occurred only during the first 3 d. This corresponds with the usual death rate of normally bred animals.

The viability of embryos of treated females of approximately the same litter size as of controls (up to sixteen embryos) is 64.4% (compared with 85% of controls), whereas the rate of survival in embryos of all treated females (including high litters also) is 66%. This indicates that embryonic death is not a result solely of excessive litter size in treated females.

Embryos of females injected with hormone, as well as of controls, were sexed after artificial and normal birth respectively. The sex ratio of males to females is 1 : 1.82 in the treated animals, whereas the controls show the usual slight imbalance in favour of males (ratio 1 : 0.96). This suggests that gonadotrophin treatment before pregnancy directly influences the distribution between the sexes.

The observed malformations are illustrated in Figs 1 and 2. Embryos of females (hormone-injected) with a litter size between fifteen and twenty-two showed postaxial oligodactylism of the forelimb. One embryo had a forelimb dysmelia of the reduction type which was also seen on late resorptions. Seven

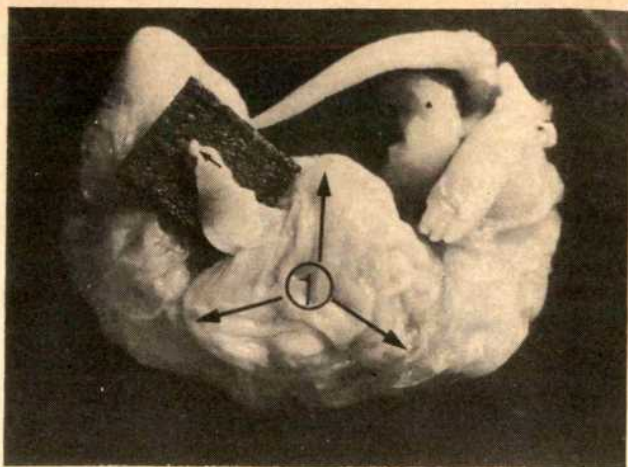


Fig. 2 Malformation of the right forepaw (dysmelia) and cystic bladder (1). This animal was dead at the time of Caesarean section. Note the absence of digits 2, 3, 4 and 5. The thumb (arrow) is suppressed to a thin structure.

of eight embryos were found to be abnormal with respect to the right forelimb (six females, one male), whereas the eighth (male) showed an aplasia of the left forelimb. The abnormalities observed in these experiments have a striking similarity to less severe lesions obtained in rats treated with acetazolamide during mid-pregnancy^{18,19} and in mice treated with 5-fluoro-2-deoxycytidine²⁰. The malformations reported here are phenocopies of the oligodactylism described by Grüneberg²¹ where, as a rule, the postaxial areas of the limb skeleton are also affected. The only difference is that in oligodactylism the left forelimbs are slightly more often affected, whereas in the observations reported here, as after treatment with acetazolamide, more right forelimbs were affected.

This study has shown that gonadotrophin treatment before pregnancy can result in statistically significant anomalies and a shifted sex ratio, as well as in a reduced survival chance after Caesarean section.

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Identification of Skin in Airborne Particulate Matter

In the assessment of airborne particulate contamination, it is necessary to identify and quantify the particle species in the environment. Many of the particles recovered from the air have been identified microscopically as being skin scales shed from humans, similar to those shown in Fig. 1. In some circumstances particles may be recovered which are fragmented and appear "dirty" and their microscopic identification then becomes difficult¹. This is especially true when airborne samples from outside air contain small fragments of leaves or the wax cuticle from plant surfaces which are similar in appearance to skin scales.

Here we describe a technique for identifying skin particles by analysis of the surface fats on the recovered particles. In this way many of the airborne particles which have been dismissed as "dust of unknown origin" are shown to have originated from the skin of humans or animals.

The composition of the cuticle and surface waxes on leaves is well documented². In most species, the hydrocarbons in the surface wax are saturated and consist predominantly of substances with an odd number of carbon atoms. In cabbage leaves, for instance, the surface wax consists of a complex mixture of long chain compounds, but some 65% of this wax is made up of only seven different straight chain compounds, all twenty-nine carbon atoms long. One compound, normal-nonacosane (n-C₂₉), makes up more than 90% of the hydrocarbon fraction. Table 1 shows the average composition of human skin surface fat taken from the forearm³.

Our skin identification technique is based on the presence of squalene in human skin and its absence from the surface layer of leaves. (As a preliminary to the analysis of samples of airborne particles, the presence of squalene on the skin surface was confirmed by the use of a Varian Aerograph 2700 gas chromatograph coupled to a Varian MAT 731 mass spectrometer and data were processed by the Varian 100 MS Spectro System.) Skin was gently scraped with a scalpel blade and the dislodged skin scales were collected. The fats were then dissolved in a known quantity of carbon disulphide and an aliquot injected into a Perkin Elmer chromatograph. The squalene content was shown to be of the order of 1% by weight of the collected skin scales (Fig. 2) and the quantities of squalene recovered by petroleum ether washing of the skin of various subjects were

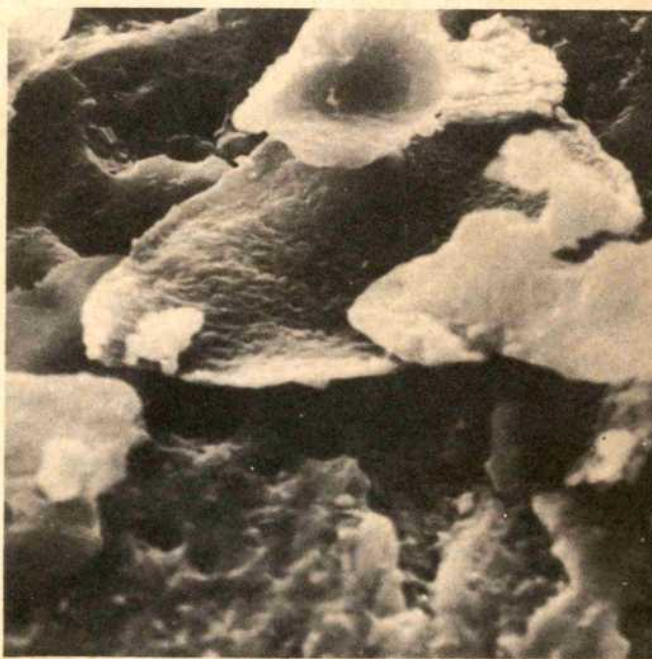


Fig. 1 Scanning electron micrograph of skin fragments some 2 to 5 µm across and 0.5 µm thick, recovered from room air.

Table 1 Composition of Average Skin Surface Fat from the Forearms of Men^a

Free fatty acids	30.0%
Triglycerides	32.5%
Straight chain wax esters	10.7%
Branch chain wax esters	
Cholesterylestes	4.3%
Cholesterol (free)	2.5%
Squalene	5%
Paraffins	7.5%
Unidentified unsaponified fat	7.5%

Table 2 The Percentage of Skin (by Weight) in the Collected Air Samples from Four Locations

Origin of samples	Particle size ranges		
	6 to 2 μm	2 to 0.7 μm	0.7 to 0.4 μm
<i>a</i> Garden	0.4	0.6	0.8
House	0.4	0.7	0.8
Laboratory corridor	1.0	0.5	0.5
<i>b</i> Underground system	5.5 to 3.5 μm	3.5 to 2 μm	2 to 0.3 μm
	10	10	10

Airborne particles were recovered from the air of various environments using either, *a*, a Casella Cascade Impactor or, *b*, an Andersen Mini-Sampler. The collection disks in these samplers were thoroughly cleaned with redistilled carbon disulphide before the sample was obtained. The particulate matter was removed from the disks by scraping with a thoroughly clean scalpel and then transferred to a small glass tube. The disks were weighed before and after the particles were removed and 5 μl of re-distilled carbon disulphide was added to the sample of particles from a microsyringe. The solvent and particles were drawn in and out of the syringe needle several times to ensure mixing before being injected into the gas chromatograph.

consistently of the order of 1 $\mu\text{g cm}^{-2}$ of skin area washed.

Samples of airborne particulates were collected from the open air of a rural area, indoors in the same rural area, from the corridors of the NIMR Laboratories in Hampstead and from the microenvironment of a passenger travelling in the London Underground system. The collected particles deposited on sampling disks in each of the sampling apparatus so that the fraction on any disk was within a well defined particle size range. Very little material was collected by the samplers for particles

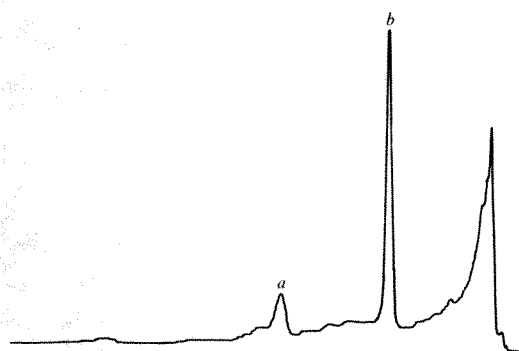


Fig. 2 Chromatogram of the fats on skin scales scraped from the body surface. The gas chromatograph used was a Perkin Elmer F-11 single column instrument with a flame ionization detector and the column was 6 foot $\times$ 3 mm internal diameter glass containing OV-1 3% on Gas Chrom Q. All injections were made directly on to the column packing. The oven temperature was 260°C isothermal and the injection port temperature 260°C. The carrier was nitrogen at 10 pounds per square inch inlet pressure. The air pressure was 25 pounds per square inch and the hydrogen pressure was 18 pounds per square inch. The solvent used was re-distilled carbon disulphide. Its purity was checked by a 4 μl injection before each set of samples was run on the chromatograph. Great care was necessary to avoid contamination at all stages of sample handling. (Simply touching the outside of the syringe needle with the fingers would give measurable amounts of squalene on the chromatogram.) All glassware was cleaned in Decon 90, rinsed thoroughly with water, dried and then rinsed with re-distilled carbon disulphide. Random checks were made to ensure the cleanliness of the glassware. *a*, Cholesterol; *b*, squalene.

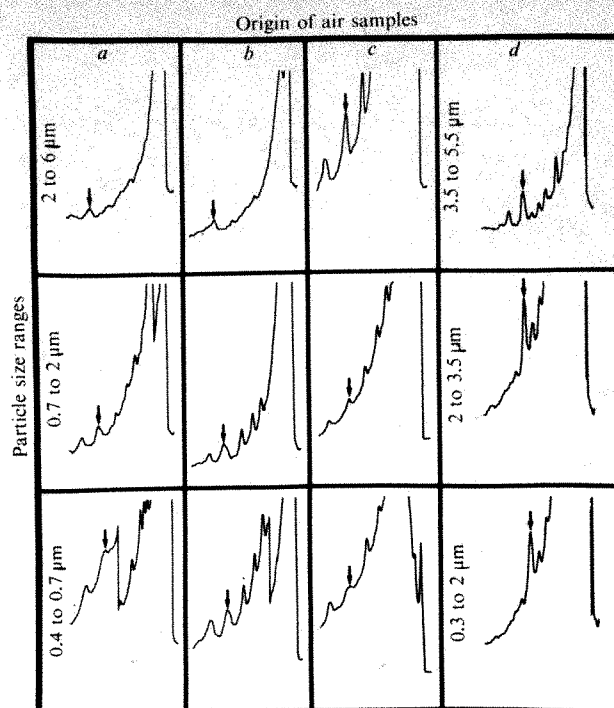


Fig. 3 Chromatograms showing the presence of squalene (arrowed) in air samples from, *a*, garden air; *b*, house air; *c*, laboratory air; *d*, air from the London Underground system.

in the largest size fraction (that is particles greater than 20 μm diameter) and these deposits were not analysed. Figure 3 shows the chromatograms produced from the airborne particulates from the four sampling locations. The percentage of skin (by weight) detected by the chromatograph (given that the squalene weight content of skin is 1%) for these locations is summarized in Table 2.

The percentage of the total collected particle weight, identified as skin by the presence of squalene, in the garden and house air was similar throughout the size range 0.4 to 6 μm , but some five times more air had to be sampled in the garden than in the house to give an adequate sample for analysis.

The total weights of skin found in the two locations are in reasonable accord with other results, to be reported elsewhere, which show that the number concentrations per unit volume of air (in the size range 0.5 to 10 μm) are consistently an order of magnitude greater in the house air than in the garden air when the size spectra of all species of airborne particles are considered.

The gas chromatograph makes possible the detection and quantification of squalene in particles recovered from the air and from the surface fats of the human skin. As this compound is absent from the surface waxes of plant leaves, the technique described here may be used in the assessment of environmental contamination caused by desquamated skin scales.

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Carbon Isotope Discrimination in Photosynthesis of CAM Plants

SUCCULENT plants capable of Crassulacean acid metabolism (CAM) show extremely variable carbon isotope discrimination ratios^{1,2}. This ratio, usually expressed as a $\delta^{13}\text{C}$ value referred to a standard³, has emerged as a useful diagnostic criterion to determine photosynthetic pathways in higher plants⁴⁻⁶. Species with the C_4 photosynthetic pathway⁶ show less negative $\delta^{13}\text{C}$ values than do species with the C_3 photosynthetic pathway. The difference in isotope discrimination is believed to be a result of the different fractionation characteristics of the primary phosphoenolpyruvate (PEP) carboxylase of C_4 plants and primary ribulosediphosphate (RuDP) carboxylase of C_3 plants⁷. Within a species, the $\delta^{13}\text{C}$ value for total carbon does not usually vary by more than $\pm 0.5\text{‰}$, and it is largely insensitive to environmental conditions during growth⁸, although the soluble components within a particular leaf may show some variation⁹. Examples of the constancy of $\delta^{13}\text{C}$ values are shown in the genus *Atriplex*, where C_4 species have less negative values (for total carbon) of -8 to -12‰ than C_3 species which range between -25 and -27‰ (ref. 8).

Here we show that the $\delta^{13}\text{C}$ value for total carbon in CAM plants undergoes significant and predictable responses to controlled growth conditions. The $\delta^{13}\text{C}$ value is correlated with other physiological events to demonstrate that the growth conditions determine the expression of C_3 -like or C_4 -like components of photosynthetic metabolism in CAM plants.

CAM plants such as *Kalanchoe daigremontiana* may fix CO_2 in the light or in the dark. Plants subjected to short hot days and long cool nights rely almost entirely on dark CO_2 fixation for net carbon gain^{10,11}. Carbon dioxide fixation in the dark in CAM plants involves a primary carboxylation of PEP to form oxaloacetate, which is reduced to malate¹². Subsequent metabolism of malic acid to carbohydrate in the light completes the analogy between these temporally separated events and the same spatially separated steps of C_4 photosynthesis^{6,13,14}.

The same CAM species may be grown in conditions of long cool days and short warm nights, in which case CO_2 fixation is largely restricted to the light period^{10,11}. During steady state photosynthesis, *K. daigremontiana* shows a light saturated CO_2 compensation point of about 50 p.p.m. in air (W. G. A., B. O. Austin, and R. O. Slatyer, in preparation). Although malate and aspartate contain a variable proportion of total radioactivity¹⁵ during short term photosynthesis in $^{14}\text{CO}_2$ pulse-chase studies show that the C_4 acids continue to accumulate label in the light (Fig. 1). The C_4 acids are end products of $^{14}\text{CO}_2$ fixation in the light¹⁵, and are not transitory intermediates as is the case with the C_4 pathway of photosynthesis. The CO_2 compensation point, and the pulse-chase behaviour of 3-phosphoglycerate and sugar phosphates (Fig. 1), suggest that CO_2 fixation in the light in *K. daigremontiana* involves direct carboxylation of RuDP and the C_3 pathway of photosynthesis.

Succulents may change their photosynthetic pathway in response to environmental influences other than temperature. Winter and von Willert¹⁶ discovered that the C_3 plant *Mesembryanthemum crystallinum* may be induced to fix CO_2 in the dark when treated with NaCl. The dark fixation of CO_2 results in a diurnal accumulation of malic acid similar to that found in CAM plants grown under short hot days and long cool nights.

We have used these two techniques, the regulation of day/night length and temperature during growth of *K. daigremontiana* and *K. blossfeldiana*, and the salinization of *M. crystallinum*, to investigate the effects of controlled environment during growth on CO_2 fixation, malate synthesis, and $\delta^{13}\text{C}$ values in CAM plants. Plants were grown in the specified conditions in CSIRO phytotron cabinets or artificially illuminated growth chambers. *M. crystallinum* was grown in soil in a greenhouse for 7 weeks before irrigating some plants with 0.35 N NaCl. Salinized and control plants were assayed 3 weeks later. Carbon dioxide fixation was followed by infrared gas analysis and diurnal changes in acid were estimated by

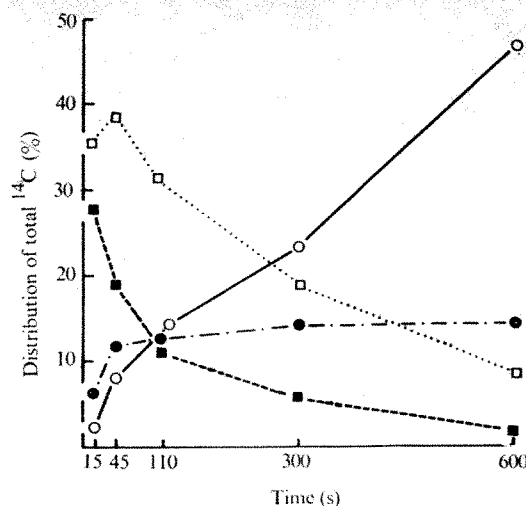


Fig. 1 Percentage distribution of ^{14}C in photosynthetic products extracted from leaves of *K. daigremontiana* exposed to $^{14}\text{CO}_2$ in a 15 s pulse, followed by a chase in $^{12}\text{CO}_2$ for up to 600 s. Leaf material was removed from plants in the 27/15°C regime of experiment 2 (Table 1) at the end of the light period. Leaf segments (2.5×4 cm) were illuminated for 10 min with $30,000 \text{ erg cm}^{-2} \text{ s}^{-1}$ of white light at 28°C before exposure to $50 \mu\text{Ci } ^{14}\text{CO}_2$ ($60 \mu\text{Ci } \mu\text{mol}^{-1}$) in a 75 ml vessel. (●), Malate + aspartate; (○), sugars; (■), sugar monophosphates + 3-PGA; (□), sugar diphosphates.

titration and direct assay for malate. The $\delta^{13}\text{C}$ value was determined by mass spectrometry after combustion of dried plant material¹⁷. Five to twenty plants were sampled in each treatment.

Table 1 shows the results of four such experiments. Treatments which permit CO_2 fixation predominantly in the light period (C_3 -like photosynthetic mode) result in small changes in malic acid content and yield more negative $\delta^{13}\text{C}$ values. Treatments which restrict CO_2 fixation predominantly to the dark period (C_4 -like photosynthetic mode) result in large changes in malic acid content and less negative $\delta^{13}\text{C}$ values. It is unlikely that the increased malic acid content is in itself responsible for the more negative $\delta^{13}\text{C}$ values, which presumably apply to all components of the tissue⁹. Duplicate determinations of the $\delta^{13}\text{C}$ value in experiments 2 and 3 show the reliability of the method when based on a large number of plant samples.

There is a good correlation between the principal mode of CO_2 fixation during growth and the $\delta^{13}\text{C}$ values. Growth dependent on dark fixation results in less negative $\delta^{13}\text{C}$ values than growth which is largely dependent on CO_2 fixation in the light. The magnitude of the change in $\delta^{13}\text{C}$ value, and absolute $\delta^{13}\text{C}$ values, display some variation between experiments and species which may be explained in terms of the conditions of the experiments. In experiment 1, for example, growth of *K. daigremontiana* on the 20/25°C regime was five-fold greater than that on the 30/15°C regime. In experiment 4, *M. crystallinum* was grown for 7 weeks in control conditions before treatment with 0.35 N NaCl. The proportion of tissue carbon laid down in the C_4 -like growth conditions of both of these experiments is smaller than that laid down in the C_3 -like conditions. The changes in $\delta^{13}\text{C}$ values in the C_4 -like treatments are thus considerably underestimated.

We conclude that CAM plants have the option of a C_3 -like or a C_4 -like mode of photosynthetic metabolism. In most conditions it is likely that a CAM plant will receive contributions from both components during its development. The proportion gained in the light or dark responds rapidly to changes in temperature on a day to day basis, as shown by Neales¹¹. The final $\delta^{13}\text{C}$ value shown by the tissue should reflect the proportion of carbon gained through each pathway during growth.

Table 1 Effects of Controlled Growth Conditions on the Photosynthetic Behaviour of Succulent Plants Capable of Crassulacean Acid Metabolism

Species and tissue	Growth period (weeks)	Temperature day/night (°C)	Day length (h)	Illumination	Photosynthetic mode	Diurnal malate change ($\mu\text{mol g}^{-1}$ fresh wt)	$\delta^{13}\text{C}$ value (‰)
1. <i>K. daigremontiana</i> plantlets	0	—	—	—	—	—	—20.1
young plants	3	20/25	8	sunlight	C ₃ -like	25	—24.0
young plants	3	30/15	8	sunlight	C ₄ -like	53	—19.8
2. <i>K. daigremontiana</i> mature leaves	10	24/19	16	sunlight + artificial*	C ₃ -like	20	—18.0, —18.4
mature leaves	10	27/15	12	artificial†	C ₄ -like	110	—13.3, —13.3
3. <i>K. blossfeldiana</i> mature leaves	12	26/20	15	sunlight + artificial*	C ₃ -like	‡	—26.4, —26.4
mature leaves	12	27/17	9	artificial†	C ₄ -like	‡	—19.1, —18.4
4. <i>M. crystallinum</i> control, mature leaves	10	glasshouse conditions	—	sunlight	C ₃ -like	0.1	—28.3
0.35 M NaCl, mature leaves	10	glasshouse conditions	—	sunlight	C ₄ -like	38	—22.5

* Approximately 6×10^6 erg $\text{cm}^{-2} \text{s}^{-1}$ (400–700 nm) with day length extended with low intensity tungsten lamps.

† Approximately 3×10^4 erg $\text{cm}^{-2} \text{s}^{-1}$ (400–700 nm) from tungsten lamps and fluorescent tubes.

‡ Not measured here, see ref. 10.

Our experiments show that a variety of environmental conditions may regulate the proportion of carbon gained by either pathway. It is likely that the availability of water may be of paramount importance. Kluge and Fischer¹⁸ showed that droughting *Bryophyllum tubiflorum* rapidly reduced its ability to fix CO₂ in the light (the C₃-like component). Consistent with these observations, we have found that droughting mature *K. daigremontiana*, grown on the 20/25° C treatment of experiment one, made the $\delta^{13}\text{C}$ value less negative. After 9 weeks of drought, the control $\delta^{13}\text{C}$ value of -22.8 ± 0.8 ‰ moved to -16.2 ± 0.3 ‰ as the plants relied increasingly on the dark CO₂ fixation; the C₄-like component of photosynthesis. Similar data have been obtained for the $\delta^{13}\text{C}$ values of *Optunia inermis* throughout its range in eastern Australia; in arid regions of central southern Queensland, $\delta^{13}\text{C}$ values for this species range between -11 and -13 ‰ and in the more temperate, higher rainfall areas of coastal southern New South Wales we have found values of -16 to -18 ‰. Environmental control of the photosynthetic options of these plants has brought about predictable changes in the $\delta^{13}\text{C}$ value.

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Accelerated Germination by Osmotic Seed Treatment

CROP seeds sown in cold soil are notoriously slow to emerge and it would obviously be desirable to shorten the time from sowing to seedling emergence and the time between the emergence of the first and the last seedling. This has occasionally been achieved by the pre-sowing seed treatment sometimes referred to as 'hardening'¹⁻³ or 'advancing'⁴ involving repeated cycles of imbibition of a carefully controlled quantity of water, followed by drying back the seeds before the radicles emerge but results have not been consistent. There have been some successful attempts to replace this method by imbibition of seeds in salt solutions⁵⁻⁷; tomato seeds thus treated for 6 d exhibit a much higher level of RNA production during germination than untreated seeds⁸.

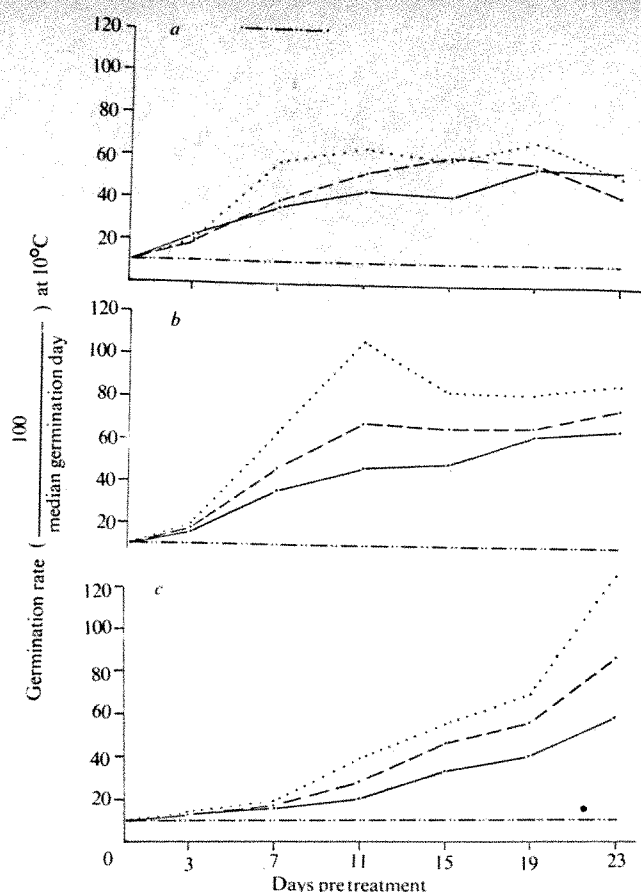


Fig. 1 Germination rate of onion seeds in response to osmotic pretreatment. Effect of water potential, temperature and duration of treatment. Seeds were placed on filter papers moistened with solutions of a polyethylene glycol of high molecular weight, Carbowax 6000 (Union Carbide) of -10 , -12.5 or -15 bar osmotic potential⁹ and at temperatures of 10 , 15 and 20°C in the dark (batches of fifty seeds on four Whatman No. 1 filter papers in 8 ml of solution per 9 cm diameter Petri dish). After 3, 7, 11, 15, 19 and 23 d, four replicates of each of the treatments were thoroughly washed and surface dried. The seeds were then placed in other Petri dishes similarly prepared but with distilled water and were allowed to germinate at 10°C in the dark. . . . , -10.0 bar osmotic potential; - - - , -12.5 bar osmotic potential; - · - · - , -15.0 bar osmotic potential; —, untreated. *a*, 20°C ; *b*, 15°C ; *c*, 10°C .

By using a polyethylene glycol of high molecular weight, we have avoided the complications of both 'hardening' and the use of salts. Promising results have been obtained in preliminary experiments on carrot (*Daucus carota* L.) and red beet (*Beta vulgaris* L.), but we report here only on onion (*Allium cepa* L.) seeds.

All osmotic pretreatments resulted in an increase in the rate of radicle emergence (Fig. 1) depending in magnitude on

all three components of the preparatory treatment, that is, osmotic potential, temperature and duration. There was no effect on the percentage of seeds germinated but certain treatment combinations permitted germination of some seeds in the osmotic solution (Table 1).

For every temperature and osmotic potential combination, increasing treatment duration initially increased the rate of subsequent germination. At 15°C and 20°C , however, an optimal duration was found beyond which there was no further benefit and in some cases an eventual decline. Almost all comparable rates of germination were lower after treatment at 20°C than 15°C . At 10°C the optimal duration may not have been reached in this experiment.

When seeds were treated at 10°C and 15°C , a lower osmotic potential resulted in a lower rate of germination and a longer treatment was needed for the seeds to reach any desired rate of germination. Treatment at the lowest temperature caused a slower increase in the rate of germination than treatment at the higher temperatures, but ultimately resulted in the highest rate achieved. The combination of -10 bar and 15°C for 11 d, however, was nearly as successful in increasing the rate of germination of the seed population as the best treatment; -10 bar at 10°C was 0.8 d, when the resulting median time from sowing to radicle emergence at a germination temperature of 10°C was 0.8 d, which compared with 9.3 d for untreated seeds (Fig. 2). It would be hard to better this result.

This technique has fascinating physiological implications,

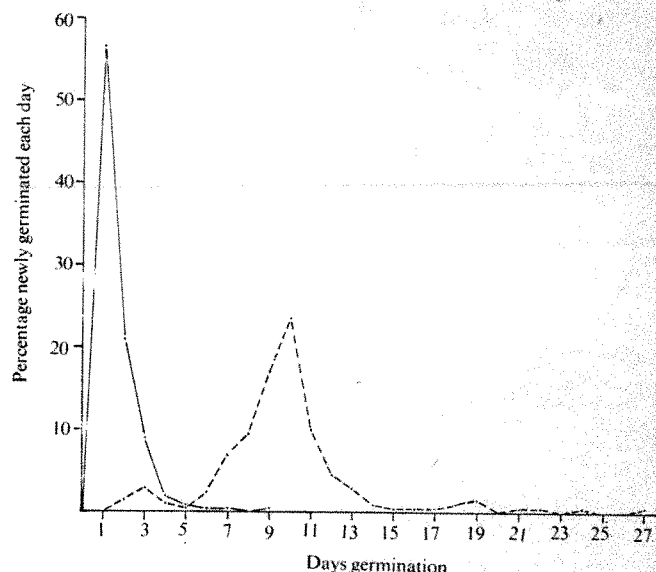


Fig. 2 Germination of onion seeds in response to 23 d osmotic pretreatment in PEG (Carbowax 6000) solution of -10 bar potential at 10°C . Germination at 10°C on filter paper moistened with water. The pretreatment increases both the rate and the uniformity of germination. —, Pretreated, washed and dried; - - -, untreated.

Table 1 Percentage Germination of Onion Seeds (cv. Excellent) During and After Osmotic Pretreatment* in PEG (Carbowax 6000)

Pretreatment Temp. ($^\circ\text{C}$)	Potential (bars)	Days					
		3	7	11	15	19	23
10	-10	0+96.0	4.0+88.0	9.0+83.5	10.5+82.0	15.0+79.0	9.0+80.5
	-12.5	0+93.5	1.0+91.0	0+91.5	6.0+86.0	2.0+85.5	3.0+88.5
	-15	0+90.5	0+94.5	0.5+93.0	1.5+92.0	1.0+85.5	1.5+89.5
15	-10	0+87.5	1.5+93.5	4.5+90.5	15.0+82.0	21.5+72.5	18.0+74.5
	-12.5	0+92.0	0+92.0	1.5+90.0	5.0+88.5	2.5+94.0	4.5+93.0
	-15	0+93.0	0+90.0	0+94.0	2.5+92.5	1.0+94.5	1.0+90.0
10	-10	0+93.5	0+92.5*	0.5+94.0	0+88.5	5.5+84.5	3.5+91.0
	-12.5	0+92.0	0+90.0	0+89.5	0+89.5	0+90.5	0.5+94.0
	-15	0+96.0	0+93.0	0+92.0	0.5+90.5	0+89.5	0+88.0
Untreated 90.0.							

* Different water potentials, temperatures and durations of treatment. Germination temperature 10°C .

and promises to be of considerable value in establishing crops from seeds sown in early spring.

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In vitro Control of *de novo* Flower, Bud, Root, and Callus Differentiation from Excised Epidermal Tissues

AMONG the plant species capable of neoformation, a much larger number are capable of root and vegetative bud formation than of direct flower neoformation. For most materials, the formation of buds or roots or flowers concerns different tissues, such as epidermis, perivascular or callus tissue of cambial origin, and each tissue maintains complex correlation with the surrounding tissues.

The study of the control of organogenetic differentiation is faced with certain difficulties because of the different tissues involved in the origin of different types of organogenesis and the complexity of the material: lack of criteria for a valid study of changes during organogenesis and for rigorous comparisons among the different types of organogenesis.

This problem was simplified when it was found that a few superficial cell layers excised and cultured *in vitro* have organogenetic potentialities which can be controlled at will. From very small explants of *Nautilocalyx lynchei* (5 mm × 2 mm), composed of one to five layers of foliar epidermal and subepidermal cells, mitoses without organogenesis (non-organogenetic differentiation), mitoses leading to the controlled formation of roots (Fig. 1) or vegetative buds (Fig. 2) (organogenetic differentiation) were induced from the same cellular layer, the epidermis, each cell of which divides¹. Thus, by the *in vitro* culture of a few superficial cell layers, it is possible to show experimentally the capacity for callus formation and *de novo* formation of roots up to then apparently inhibited. In leaf or stem fragments, root formation is confined to perivascular tissue.

With such materials, certain fundamental problems in organogenesis, which are difficult to study using relatively large organ fragments, can be examined. For example, for *Nautilocalyx*, where bud and root neoformations arise from epidermal cells, it would be possible to study the evolution and distribution of organogenetic centres by observing the thousands of cells on the epidermal surface to determine whether there is a special mode of distribution of these centres in relation to the presence of basal hair cells or stomata.

To the potentialities for bud, root and callus formation, we were able to add the direct *de novo* formation of floral buds on the explant without intermediate callus or leaf

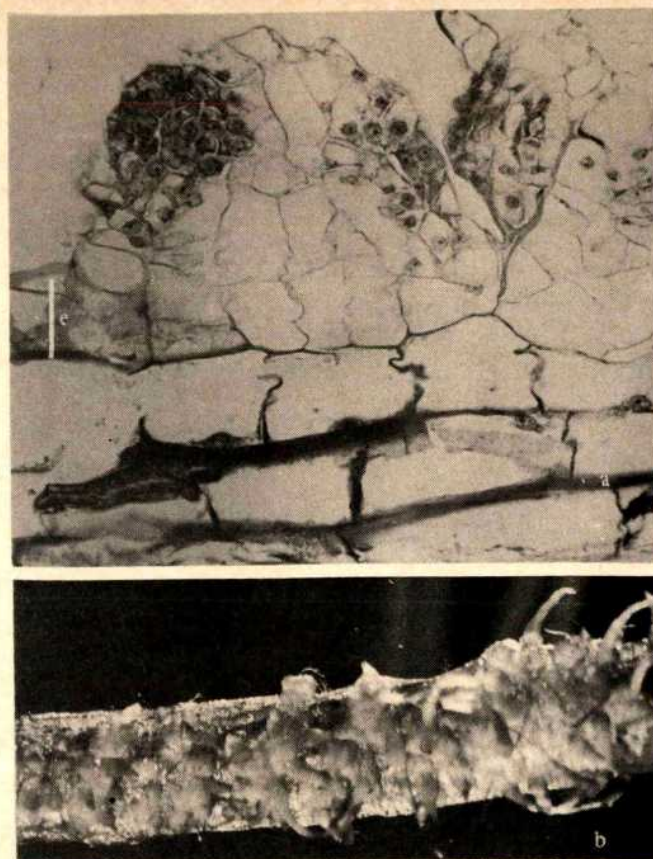


Fig. 1 a, Longitudinal section of an explant of *Nautilocalyx* showing the epidermal origin of the root primordia organized *de novo* from divided epidermal cells. (×160.) b, *De novo* formation of roots from epidermal tissue explants after 37 d. e, Epidermis.

formation by applying the techniques described for *Nautilocalyx* to explants composed of three to five layers of epidermal and subepidermal cells excised from floral ramifications of *Nicotiana tabacum* "W.38". These explants are excised with a scalpel from floral ramifications previously disinfected in a 7% hypochlorite solution for 10 min, and planted on an aseptic culture medium composed of mineral elements, vitamins, auxin, cytokinin and sucrose.

Depending on the relative concentrations of the auxin, cytokinin and sucrose and on certain environmental factors, such as light and temperature, different types of differentiation can be induced in 10 to 14 d: callus formation which has been maintained without organogenesis for 2 yr, root formation, vegetative shoot formation and floral bud formation (Fig. 3). This last type of organogenetic differentiation is the most interesting. It implies that stimulation of mitoses takes place in cells which had lost

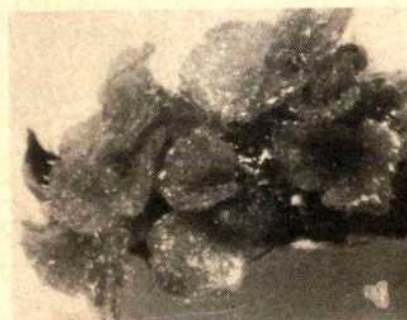


Fig. 2 Explant showing the *de novo* shoot formation, the surface covered with buds after 37 d. (×8.)

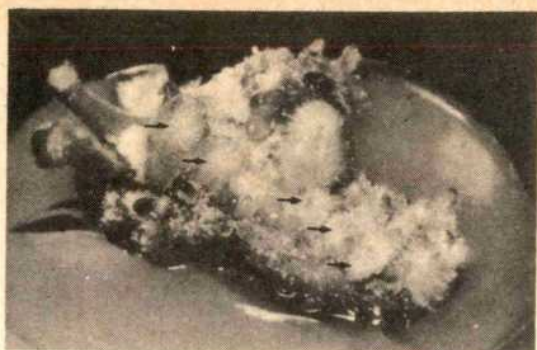


Fig. 3 Surface of the explant covered with floral buds formed *de novo* (arrows). 20 d stage. ($\times 2.5$.)

their capacity to divide, and that, after a short phase of production of floral parts, meiosis occurs.

Up to a certain stage, each one of these types of organogenesis can be converted into a different one. After this point, differentiation is irreversible.

An analysis at the cellular level has established that all these types of differentiation originate from the same cellular layer, the subepidermal layer, each cell of which participates in the differentiation. It is thus relatively easy to study the cellular and molecular modifications which occur in this layer during each type of organogenetic differentiation or at the exact moment of conversion from one programme to another.

These new experimental systems, with others developed in our research group, will facilitate a more precise approach to the determinism of differentiation in pluricellular systems by their simplicity and homogeneity.

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¹ Tran Thanh Van, M., and Drira, A., *Colloques int. Cent. natn. Rech. scient.*, **193**, 169 (1970).

Locomotor Affinities of *Hominoid* Tali from Kenya

A CONTRIBUTION to this journal¹ is among several that have attracted criticism from Oxnard². This communication has two objects; first, to reply to comments by Oxnard which relate to a possible ambiguity in the earlier communication; second, to present the results of a new analysis which provide additional evidence for the interpretation of the mode of locomotion of East African dryopithecines.

The object of the earlier work was to test the hypothesis, formulated by the late L. S. B. Leakey³, that two tali, one found at Songhor (CMH 145) and the other at Rusinga (CMH 147), may belong to the taxon "*Kenyapithecus africanus*", a putative early hominid. A multivariate canonical analysis, using extant hominid and pongid comparative material⁴, was performed. The first canonical axis produced clustering of the groups which

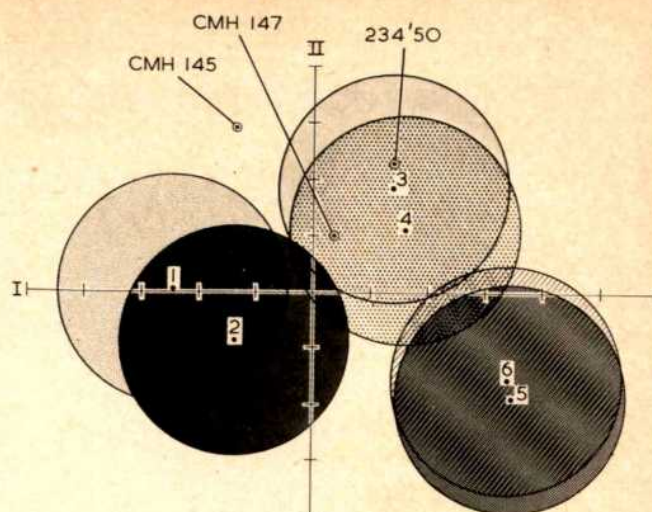


Fig. 1 Plot of canonical axes I and II. Circles are drawn with a radius of two eigenvalues. 1, *Gorilla*; 2, *Pan*; 3, *Papio*; 4, *Cercopithecus* (*mona* and *nictitans*); 5, *Colobus*; 6, *Pongo*.

corresponded to accepted locomotor classifications based on anatomical and behavioural analyses. This demonstrated the efficacy of the canonical coefficients of the first axis as locomotor discriminators. By contrast, the second and higher canonical axes failed to distinguish between "knuckle-walking" apes and bipeds. Thus, *a posteriori*, the canonical coefficients of the second and higher axes had no individual usefulness as discriminants between the extant locomotor groups.

The canonical coefficients for the first canonical axis were then used to process the data for the two fossil tali and an additional talus from Rusinga (234'50), and it was found that these tali lay closer to the knuckle-walking locomotor category than to the bipeds. This was taken as evidence that complemented and substantiated earlier morphological assessments that these tali are pongid or dryopithecine and not hominid.

Oxnard has suggested that the D^2 values indicate the affinity of the fossil tali for the knuckle-walking locomotor group confined to the first canonical axis, and is dependent on the limited choice of comparative groups. He continues, "the *Proconsul* tali are completely unlike African apes rather than similar as previously assessed", presumably because the sum total of the individually insignificant deviations in the second and higher axes place the fossils several units of Generalized Distance away from the extant apes.

Therefore, in order to investigate further the functional relationships of these fossil tali, and to attempt to reconcile these seemingly opposed views, a new canonical analysis has been performed.

The new comparative groups, with their locomotor classifications, are listed in Table 1. An attempt has been made, within the limits of available material, to improve the resolution of this technique by including a wider variety of sub-human Old World primate locomotor modes. Mahalanobis D^2 distances and canonical variates were calculated from measurements on the tali as outlined previously⁴. Seven significant canonical axes, of which the first three contained 97% of the total variability, were produced; subsequent axes did not individually contribute significantly to the discrimination.

Table 1 Comparative Groups

Groups	1 <i>Gorilla</i>	2 <i>Pan</i>	3 <i>Papio</i>	4 <i>Cercopithecus</i> <i>mona/nictitans</i>	5 <i>Colobus</i>	6 <i>Pongo</i>
No. of specimens	50	50	42	17	16	15
Locomotor classification	Knuckle walker	Knuckle walker	Quadruped	Quadruped	Quadruped (with leaping)	Brachiator (hind limb grasping)

Table 2 D^2 Distances and Probability Levels between Group Means

Groups	1	2	3	4	5
2	3.4 ($<0.1\%$)				
3	18.8 ($<0.1\%$)	14.9 ($<0.1\%$)			
4	18.2 ($<0.1\%$)	14.2 ($<0.1\%$)	1.6 (1.0%)		
5	47.4 ($<0.1\%$)	32.7 ($<0.1\%$)	25.4 ($<0.1\%$)	20.5 ($<0.1\%$)	
6	47.1 ($<0.1\%$)	34.5 ($<0.1\%$)	26.9 ($<0.1\%$)	21.2 ($<0.1\%$)	34.3 ($<0.1\%$)

eschew the former two groups and cluster with the combined knuckle-walking and quadrupedal groups. In axis I particularly, CMH 145 behaves differently from the other two fossil tali.

The Mahalanobis D^2 distances between the group means, with their probability levels, are given in Table 2; the D^2 distances of the fossil tali from the extant group means, along with probability levels, are given in Table 3. These distances confirm the dissimilarity between the fossil tali and those of both *Pongo* and *Colobus*. One talus, CMH 145, has no close affinity with any of the extant locomotor groups. The other two tali are closely related to tali of the quadrupedal group (*Papio* and *Cercopithecus*) and one, CMH 147, shows some affinity with the knuckle-walking tali.

Table 3 D^2 Distances and Probability Levels between Groups and Special Cases

	Comparative groups					
	1	2	3	4	5	6
	<i>Gorilla</i>	<i>Pan</i>	<i>Papio</i>	<i>Cercopithecus</i>	<i>Colobus</i>	<i>Pongo</i>
Fossil tali						
CMH 145	13.7 (5.0%)	18.4 (1.0%)	13.5 (5.0%)	14.8 (5.0%)	64.2 ($<0.5\%$)	50.5 ($<0.5\%$)
CMH 147	12.2 (10.0%)	8.7 (25.0%)	3.5 (85.0%)	5.7 (50.0%)	26.5 ($<0.5\%$)	30.6 ($<0.5\%$)
234'50	21.3 ($<0.5\%$)	17.7 (1.0%)	0.5 (99.0%)	2.5 (90.0%)	29.6 ($<0.5\%$)	29.7 ($<0.5\%$)

A plot of canonical axes I and II (Fig. 1) shows a clear separation of the knuckle-walking and quadrupedal locomotor groups, with no such separation between *Pongo* and *Colobus*. A further plot of axes II and III (Fig. 2) shows that axis III is a strong discriminator between *Pongo* and *Colobus* but has little effect on the other groups. Thus, between them these three axes produce a three-dimensional separation of extant samples that is consistent with current locomotor classifications; tali coming from primates with different locomotor modes are rarely confused in this analysis.

Subject to certain limitations, as outlined by Gower⁵, the canonical coefficients derived from the analysis can be used to determine the position of samples of extinct fossil primate genera in the same multivariate space.

The positions of the fossil tali have been plotted for the first three axes. In axis I (which effectively discriminates between a knuckle-walking and quadrupedal gait) two of the fossil tali are clustered with the quadrupeds. The third talus, CMH 145, is not associated with any extant locomotor group. In axis III, which successfully separates *Pongo* and *Colobus* from each other, from the quadrupeds and from the knuckle walkers, all three fossils

Thus, by focusing attention on how the talus varies between locomotor modes in a more extensive series of sub-human primate genera than were used in the earlier analysis, two of the fossil tali appear to show the same morphological features as cercopithecoïd quadrupeds. These quadrupeds are characterized by a relatively long anterior tarsal segment, associated with the use of the metatarsal heads as the fulcrum for their propulsive movement. Their body weight is transmitted almost exclusively by the trochlear surface of the talus, whereas in the ground-adapted pongids the laterally projecting fibular articular facets, with corresponding modifications of the fibula, indicate a lateral shift in the axis of weight transmission. When the canonical weights are examined for variate I, a long talar neck and an insignificant fibular facet are indeed parameters which discriminate between the quadrupeds and the knuckle-walkers.

In summary, this analysis confirms that these fossil tali are more like the tali of knuckle walkers than bipeds. As suggested by Oxnard, however, the similarity has been shown to be relative because finer locomotor discrimination reveals that the two fossil tali from Rusinga show a greater, and indeed significant, affinity with tali of the quadrupeds *Papio* and *Cercopithecus*. This confirms the earlier morphological assessment of Le Gros Clark and Leakey⁶ and suggests that the inclusion of these Miocene tali in the locomotor group represented by extant knuckle-walking pongids may be premature. Moreover, the behaviour of CMH 145 in the analysis is additional evidence for Pilbeam's contention⁷ that this specimen may belong to a different species from that of the tali from Rusinga.

I thank Professors E. H. Ashton and M. H. Day for their helpful comments, Mr G. B. Newman for continued statistical advice and Miss Leader for typing the manuscript.

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¹ Day, M. H., and Wood, B. A., *Nature*, **222**, 591 (1969).

² Oxnard, C. E., *Am. J. Phys. Anthropol.*, **37**, 3 (1972).

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⁷ Pilbeam, D., *Nature*, **223**, 648 (1969).

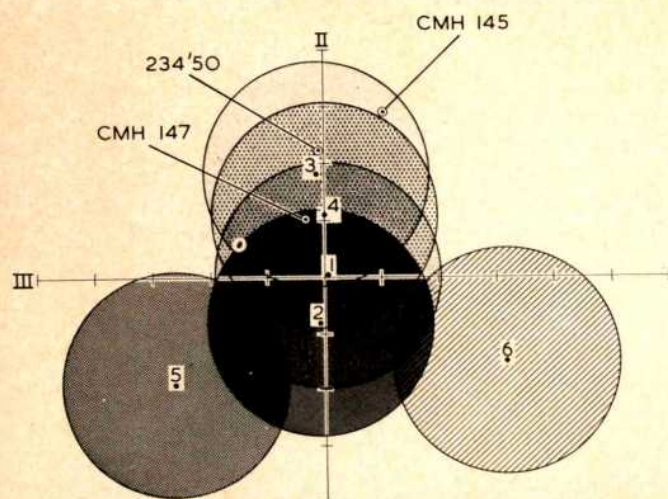


Fig. 2 Plot of canonical axes II and III. Circles are drawn with a radius of two eigenvalues. Comparative groups as in Fig. 1.

BOOK REVIEWS

Primate Evolution

Evolution of Primates: An Introduction to the Biology of Man. By A. B. Chiarelli. Pp. xi+354. (Academic: New York and London, April 1973.) £7.20.

THE publishers announce this as "probably the only comprehensive treatment on primate evolution to be compiled", which is odd because Academic Press have recently issued a much more useful book on virtually the same subject^{1,2}; and most of the wide field approached by Professor Chiarelli is adequately covered in a well written textbook which has already seen several years of service³. It is, indeed, an enormous undertaking to deal with genetics (from the molecular level upwards), speciation, living and fossil primates and the emergence of man all in one volume. However, there is always the danger with such a wide-ranging approach that depth of treatment and command of theoretical issues will be wanting, and Professor Chiarelli has unfortunately failed to cope with the task that he set himself.

Although concerned with the central theme of primate evolution, there is no discussion in the text of the methods used to establish evolutionary relationships. The fundamental concepts of homology and convergence, for example, are left unmentioned. Instead, Chiarelli uses the simple model of the living primates as a graded series of arrested ancestral stages: "In fact, prosimians, monkeys and anthropoid apes may represent the survival of stages reached in the past by human ancestors". In line with this, it is also stated that "comparative anatomists and palaeontologists now generally agree that the tree shrew can serve, *cum grano salis*, as an example of the first phase of the evolution of the primates". First, it is a vast oversimplification to imply that tree shrews simply ceased to evolve some 70 million years ago. Second, it should at least be mentioned that several authorities⁴⁻⁷ have now rejected the hypothesis that tree shrews are related to primates.

Even if used as a model for primate evolution, tree shrews are of marginal importance; but it is nevertheless desirable to describe them accurately. Yet the fossil *Anagale*, which is in any case an unlikely relative of tree shrews^{8,9}, is vaguely referred to as "Oligocene fossil *Ptilocercus* from Mongolia". And when it is stated that the living tree shrews are "among the smallest existing mammals, very lively and aggressive,

and as their metabolic rate is very high they eat voraciously", it is apparent that Chiarelli has confused the Soricidae with the Tupaiidae. We are also told that the tree shrews have eyes "placed at right angles to each other".

Slips of this kind are, unfortunately, abundant. The aye-aye, for instance, is said to live on the juice sucked from sugar-cane, and this admittedly bizarre lemur is granted two different dental formulae on pages 59 and 157. We are informed that, for the lemurs in general, "their intellectual capacity has not increased during their evolution from the time they arrived in Madagascar", and it is stated that Palaeocene and Eocene fossil relatives have been found in Africa. Palaeontologists will also be surprised to see that the map of world distribution of fossil primates omits the entire New World.

Although the description of the better known simians is generally more accurate, it is unsettling to find that Chiarelli—apparently on the basis of superficial karyological and serological similarities—takes the unusual step of classifying the gibbon with cercopithecoïd monkeys rather than with the apes. Interpretation of similarities of this kind is by no means simple, and in an intended textbook such sweeping revision of a widely used classification deserves full discussion. In any event, on page 141 Chiarelli overlooks his revision and reverts to placing the gibbon (misprinted as *Hyloteles*) in the Hominoidea.

The sphere of hominid evolution fares no better. On page 236, a maxilla attributed to *Ramapithecus* is mislabelled and printed upside down, and Chiarelli states (perhaps through the agency of yet another misprint) that this genus displays the most hominoid characteristics within the dryopithecine radiation. With the later hominids, in spite of the fact that many recent authors have followed a greatly clarified scheme^{10,11}, Chiarelli revives the now obsolete proliferation of genus and species names. Apart from referring to *Homo erectus* exclusively as "*Pithecanthropus*" and to the *H. erectus*/*H. sapiens* transition stage as "*Protanthropus*", the term "*Palaeanthropus*" is used as if it were a genus name for forms which are also referred to as *Homo* species. Nowadays, this kind of confusion over nomenclature is only justifiable for forms of questionable taxonomic status, such as "*Homo habilis*"

from Olduvai; yet this particular form is totally omitted from the discussion of hominid evolution.

Chiarelli's primary research area is that of genetics and karyology, and chapters on these aspects to some extent compensate for failings elsewhere. Even these chapters, however, are not without serious faults. For example, the discussion of chromosomal evolution which is given with remarkable brevity in chapter 2 is not followed until chapter 11 with the actual evidence for primates. The resulting gap in the train of thought is compounded by errors of omission. There is no definition of metacentric or submetacentric chromosomes, though distinction of these from acrocentrics is fundamental to the understanding of chromosomal evolution. Again, Chiarelli resorts to the concept of arrested ancestral stages in referring to evolutionary processes: "In fact, although it is not possible to study the karyotype of the ancestors of living species, the study of the karyotype of the latter furnished many examples of the stages through which karyotypes have passed during their evolution".

Similar deficiencies occur in the treatment of genetics. For example, two maps (on pages 113 and 115) indicate totally different I^B gene frequency distributions in Europe for the ABO blood group system. It is also stated that "the number of amino acids which make up a protein normally does not exceed 20-25", which will misleadingly indicate to some readers that all protein chains are very short, rather than that there are usually 20-25 different kinds of amino acid involved. Again, a fairly competent description of haemoglobin evolution is spoiled on page 105 by confusion over mutation rates and misprinting of the Greek symbols for haemoglobin chains. Finally, for the really crucial developing issue of tree-building using basic biochemical data, the reader is supposed to decipher the following: "In fact, at first approximation, the amount of divergence between two species can be measured by counting the ratio of the number of homologues that have a different amino acid".

There is always a possibility that recitation of individual errors may mask the true merits of a book, and it must in all fairness be said that Professor Chiarelli has exhibited an enormous range of interests and a very broad (if inaccurate) spectrum of knowledge. Two facts are certain, however; treatment of some of the subjects indicates a quite inadequate grasp of the material, and the book as a whole has been pro-

duced with a surprising lack of attention to detail. There are numerous errors of fact, partly because of the large number of printing faults, and the translation is in places not entirely clear. Even the arrangement of the chapters seems to be somewhat haphazard ("The Concept of the Species" and "Evolution of Species" are unaccountably separated by "The Living Primates"). Finally, there is frequent omission of key references from the lists at the ends of the chapters, numerous figures are reproduced without acknowledgment of the source, and the index is insufficient. In short, in spite of the valiant attempt to cover an enormous field, this book is so poorly produced that it will merely serve to confuse students taking courses in primatology.

R. D. MARTIN

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- ² Hill, W. C. O., *Evolutionary Biology of the Primates* (Academic Press, London and New York, 1972).
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- ⁴ Romer, A. S., *Vertebrate Palaeontology*, 3rd ed. (University of Chicago Press, Chicago, 1966).
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- ⁹ van Valen, L., *Evolution*, 18, 484 (1964).
- ¹⁰ Pilbeam, D., *The Ascent of Man* (Collier-Macmillan, New York, 1972).
- ¹¹ Tattersall, I., *Man's Ancestors* (Murray, London, 1970).

Predicting Technology

Technological Planning and Social Futures. By Erich Jantsch. Pp. xiv+256. (Cassell/Associated Business Programmes: London, March 1972.) £4.50.

THIS book is a masterpiece of overstatement. The author suffers a little from the illusion, common amongst enthusiastic proponents of complex management techniques, that the methods advocated are already successfully and widely practised in government and industry, or soon could be. Thus, for example, the book repeatedly refers to the experience of PPBS as though it played an extremely important part in the decision making of the United States government. No one would ever guess from this set of essays that the general experience of PPBS, however worthy the concept may be, has been one of disillusion, or that it has been largely discarded and down-graded. Even more important, it would apparently never occur to the author that there is more to be learnt about US policy making from the Watergate hearings than from PPBS or PERT.

Similarly, in the case of industry

there is a gross overestimation of the role of "technological forecasting." All the empirical evidence shows that its actual influence on decision making both in America and Europe today is very slight. Few firms employ "technological forecasters", and those which do, take their accountants' advice far more seriously.

Only when he reaches the level of world decision making does a greater degree of realism creep in, although even here Jantsch plays with the notion of the "world corporations" filling the vacuum of rational global policy making. By and large, however, he recognizes that nation states and international corporations do not at present adopt a standpoint of global responsibility, but one of self-interest. This leads him to a position of extreme pessimism, as he accepts uncritically the naïve models of Forrester on resource depletion, population and pollution. Chapter 14 is a reprint of his review of Forrester's book. Since he irritatingly equates "rationality" with the adoption of "system dynamics" by policy makers, it is hardly surprising that this chapter strikes a "Gottterdammerung" note markedly contrasting with the earlier chapters.

The style is somewhat ponderous and opaque. It compares in this respect rather unfavourably with the lucidity, scholarship and common sense of Vickers' discussion of similar problems, or Bright's clear, practical explanations or Gabor's lively normative approach to the choice of technology and future social change. Impatience with the unsatisfactory progress and narrowness of all the social sciences is quite understandable and legitimate, but Jantsch is too often inclined to substitute the box-diagram or the organisation chart. Not surprisingly, he has a considerable affinity with Forrester, the leading exponent of the universal application of system dynamics to social problems of all kinds. He shares with Forrester, too, an exaggerated respect for the capacity of American corporations to find solutions for social problems, whether at home or abroad.

All of which is a great pity, because underneath the jargon there is a nugget of gold. Whilst Jantsch suffers in full measure from some of the typical faults of the systems engineer in discussing social systems, his book also has the great virtues of this approach. He cuts through the trees and sees the wood as well. Many of his observations about policy making, new institutions and the complementary relationship of extrapolative and normative forecasting are extremely important.

Interdisciplinary research and functionally-based decision making are both highly desirable in many modern institutions. Although he exaggerates their

contemporary influence, some of the methods and reforms which he advocates are urgently needed. If he could summarize the main theme of these essays, and concentrate on the essential message, it would be a shorter book, but a much better one.

C. FREEMAN

Protective Mixture

Radiation Protection: A Guide for Scientists and Physicians. By J. Shapiro. Pp. xx+339. (Harvard University: Cambridge, Massachusetts; Oxford University: London, 1972.) £7.50 boards; £3.50 paper.

THE prospective author of a textbook or manual on radiation protection is required to provide a proper mixture of various disciplines and practices—physics, chemistry, biology, medicine, instrumentation, public relations, legislation and so on. To be truly comprehensive the mixture must be absolutely right but the author has a certain freedom in selecting the extent and the academic level of his compilation.

Dr Shapiro has aimed at a wide range of readers, including "physicians, research scientists, engineers and technicians". Part 1 is a historical prologue ranging from the primordial through the discovery of radiation to a statement of the need for radiation protection and the extraordinary measures—technical and legislative—that are necessary. Part 2 is offered as the core of the manual. It deals with the energy imparted by ionizing particles; with beta, gamma and other radiations; dose from external and internal sources and the significance relative to radiation standards, biological effects and natural background; and the calculation of radiation hazard. In the remaining parts (3-6) the following topics are covered successively: dose calculations; radiation measurements; protocol for users of radionuclides (necessary but hardly exciting); and considerations of public health (this provides valuable perspectives).

The coverage is complete, the style simple, the order logical and the whole easy to read. It is possible to criticize the disproportion in the treatment (under "Radiation Measurements") of G-M and scintillation counters (thirty pages) and that of ionization chambers (three pages). To test the academic level of this book I tried it on a young pre-university science student. He found the text intelligible and the calculations quite easy. He would have appreciated more rigorous mathematical treatments of some of the cases, inserted perhaps as appendices. This is a good manual, however, suitable mainly for the technician but with something in it for specialists from the other disciplines.

D. H. PEIRSON

NEW BOOKS FROM ELSEVIER

ATLAS OF THE TEXTURAL PATTERNS OF GRANITES, GNEISSES, AND ASSOCIATED ROCK TYPES

by **S. S. Augustithis**, Professor of Mineralogy, Petrography, Geology, National Technical University of Athens, Greece.

1973. 390 pages. Dfl. 160.00 (about US\$61.50)

The origin of granites has been a controversial subject for centuries. It is believed that a better understanding of the problem can only be achieved through observation of the textural patterns of rocks and their interpretation on the basis of the concept of comparative anatomy. With this in mind, the author has compiled an Atlas, containing 690 illustrations, which presents, compares and genetically interprets the most common textures in granites, gneisses and granitic rocks. It shows the wide spectrum of textural possibilities and their possible diverse origins.

THE RUGOSE CORAL GENERA

by **G. Cotton**, Blakedown, Kidderminster, England.

1973. 360 pages. Dfl. 130.00 (about US\$50.00)

For the first time condensed but complete diagnoses of Rugose Coral general and subgenera, and their type species, have been compiled in alphabetical order and in modern English terminology. The book is an up-to-date reference work and should be held by all major libraries, universities, geological surveys and prospecting companies throughout the world.

THEORY OF THE EARTH'S GRAVITY FIELD

by **M. Pick, J. Pícha** and **V. Vyskocil**, Geophysical Institute, Czechoslovak Academy of Science, Prague.

1973. 538 pages. Dfl. 96.00 (about US\$36.90)

CONTENTS:

Newton's theory of potential. Potential of some simple formations, approximate in shape to the figure of the earth. Equipotential surfaces. Reductions. Absolute gravity measurements. Relative measurements of the acceleration of gravity. Measurements of the second derivatives of the gravity potential. Some comments on the anomalous gravity field. Gravimetry and the internal structure of the earth. The geoid. Determination of the figure of the earth without considering hypotheses about its internal composition. Time variations of the gravity field. Observations of tides of the Earth's crust. Fundamental mathematical principles of gravimetric interpretation. Substitution of the Earth's body by a reference surface. Astronomical and astrogravimetric levelling.

THE OPAQUE MINERALS IN STONY METEORITES

by **P. Ramdohr**, Mineralogical and Petrological Institute, University of Heidelberg, Germany.

1973. 246 pages. Dfl. 65.00 (about US\$25.00)

The aim of this work is to provide a general survey of ore minerals occurring in stone meteorites. The author demonstrates that the investigation of carefully prepared polished sections is an excellent method of providing a clear picture of intergrowth structures. The book is based on the ore microscopic investigation of approximately 500 high-quality polished sections from 350 "falls". The results proved the subject to be far more complex than had been anticipated—15 of 35 different opaque components being completely new, with a further seven not previously known to occur in meteorites. Moreover, the existence (formerly doubted) of several ore minerals known only as extreme rarities has now been established.

GEOCHEMICAL TABLES

by **H. J. Rösler** and **H. Lange**.

1972. 468 pages. Dfl. 80.00 (about US\$30.80)

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by Ursula W. Goodenough and Robert Paul Levine, Harvard University
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edited by Willis H. Johnson, Wabash College, and William C. Steere, New York Botanical Garden

This outstanding collection of fourteen articles is written as a supplementary textbook for introductory biology or environmental ecology courses. All but two of the articles were especially written for this collection by leaders in their respective fields. The articles include: basic background, problems of the human population, the major aspects of environmental pollution, the concentration of these problems in the urban area, what scientists and the government are doing to alleviate these problems, and a humanistic viewpoint on THE ENVIRONMENTAL CHALLENGE. A biographical sketch of each author is given and additional references may be found at the end of each article.

December, 1973/384 pages/\$6.00 (tent.)/Paper

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Immunochemistry

Advanced Immunochemistry. By Eugene D. Day. Pp. xvi+447. (Williams and Wilkins: Baltimore, Maryland, 1972.) \$19.

As suggested by the title, some prior knowledge of immunology is required to appreciate this book fully. The first half of the book deals with the structure of antibodies under four headings—"Light Chains of Immunoglobulins", "Heavy Chains of Immunoglobulins", "Sizes and Shapes of the Immunoglobulins" and "The Antibody Binding Site". In each chapter the past work (particularly from the 1950s-1960s) is introduced and leads to our present state of knowledge (and problems). The second half of the book deals with the reactions of antibodies. Besides the expected applications of law of mass action to reactions of antibodies with haptens and multivalent antigens, there is a very well written and concise chapter on the active centres of multivalent antigens.

Obviously a book bearing this title and running for only 401 pages (exclusive of index) will leave out certain aspects of the subject. The author has pre-empted the words of the critic, however, by mentioning most of these in the last chapter. The first half of the book deserves unqualified approval for its concise and logical presentation of our knowledge up to about the beginning of 1971. It will be very welcome for final degree students specializing in immunology, for people who want their immunological knowledge brought up to date, and of course for PhD students for its review of the development of the various topics. The second half is not so impressive simply because most of the information is available in other books and the information it contains has been around for a longer period of time. But apart from a spelling mistake on page 391, it is a useful review of the subject.

C. A. KING

Sequencing RNA

Determination of Sequences in RNA. By G. G. Brownlee. (Laboratory Techniques in Biochemistry and Molecular Biology, Volume 3, Part I.) Pp. 265. Edited by T. S. Work and E. Work. (North-Holland: Amsterdam, 1972.) £13.30.

Nucleic Acid Sequence Analysis. By Stanley Mandeles. Pp. 282. (Columbia University: New York and London, February 1973.) £7.

In recent years great progress has been made in the field of nucleic acid sequencing. Besides the two classical techniques which opened the way to such studies, DEAE chromatography and the fingerprinting method, there are now many modifications in use for

investigating large RNA molecules. New approaches have also been introduced, based on copying *in vitro* RNA or DNA and combining the former analytical techniques with nearest neighbour determination and with kinetic analysis of synchronously synthesized fragments of RNA. The number of RNAs with at least partially known sequences is ever increasing and promising attempts have been made also to apply sequencing techniques to some DNA molecules. A comprehensive review in this field has indeed been needed for a long time and can be expected to be very helpful both to scientists familiar with some aspects of these problems and to those intending to start now nucleotide sequence analysis. It is therefore very welcome that two monographs on RNA sequencing have been published at approximately the same time.

Brownlee's book deals mainly with the two classical methods, Holley's column chromatography and Sanger's fingerprinting technique, and mentions briefly some new approaches involving *in vitro* labelling of RNAs. After a short introduction, he describes in detail the enzymic digestion and chromatographic fractionation techniques used in studying the structure of non-radioactive RNAs and the analytical methods for establishing the structure of the digestion products. Chapters 3-6 give a very comprehensive description of the fingerprinting technique, including technical details, alternative methods, diagrams showing the electrophoretic mobilities of different oligonucleotides and their degradation products. Chapter 5 is perhaps a too lengthy presentation of the sequencing of 5S RNA but it discusses also many modifications of the original technique and gives a useful illustration of the practical application of different analytical methods. Chapters 7 and 8 deal with some special problems, like minor bases and terminal sequences, while chapter 9 summarizes briefly some more recent methods involving *in vitro* labelling of RNAs.

Throughout the work the practical side of the problems is emphasized, and results are discussed only as far as they facilitate the understanding of the methods used. In addition, there is a very useful appendix, giving further details about the exact conditions for labelling, isolating, fractionating, digesting RNAs, mentioning even the suppliers of equipment, enzyme preparations and other special chemicals used. The book is certainly a very useful manual, enabling the reader to set up a suitably equipped laboratory and start sequence studies on RNA.

The intentions of Mandeles's book seem different. He reviews a much wider field of sequence work, covering

at least the principles of almost all techniques ever used for partial or total sequence determination. He even includes early approaches which had rather limited use and a chapter on physical methods which are at present not suited for sequence studies but might be further developed and possibly used in the future for such purposes. The first nine chapters describe the principle and occasionally also some practical details of all the sequencing methods applied to RNA; chapters 10 and 11 give practical description of several techniques used in RNA research, from isolation techniques of RNA to analysis of some small degradation products. The choice of techniques presented in this latter part is not very fortunate: some simple, widely known procedures are described in detail while some specialized techniques are mentioned rather briefly. The last chapter summarizes the results of RNA sequencing: the structures of a great number of RNAs, as known today, are shown.

As the first review covering this whole field the book is certainly of considerable interest. It is not very well suited, however, to be used as a manual or as a guide to find the best technique for a particular sequencing problem. This is partly because the practical information is sometimes insufficient, partly because different methods are not always critically compared and evaluated with respect to their application to different problems.

M. SZEKELY

Inorganic Systems

The Constitution of Inorganic Compounds: Atomic Quantum Mechanics—Metals and Intermetallic Compounds. By John L. T. Waugh. Pp. xv+797. (Wiley: New York and London, August 1972.) £12.50.

THIS is an immense book, but it is only the first of two volumes devoted to inorganic molecules and solids. This first volume concentrates on the fundamentals of quantum theory, so that by page 797 the reader has just been prepared for a subsequent study of inorganic systems. It is a pity that both volumes could not have been published simultaneously, for one could then see more clearly the rationale of the choices of topic in volume 1.

In brief the author presupposes no prior knowledge of quantum theory. He introduces it from scratch, developing the general principles of the wave equation, operators, mean values, particle-in-a-box, hydrogen atom, and so on, following rather standard analysis. There follow chapters on variation and perturbation methods, spin, and atomic structure. By now we are at page 379 and halfway through the book. The second half is devoted to the metallic

state, band structure, Brillouin zones and a little about intermetallic compounds.

This is a formidable amount of material, especially when one sees what the author means when he writes in the preface that he wants to discuss inorganic systems "without simply stating results". He has certainly achieved this aim: there are three pages showing line by line how to pass from Cartesian to spherical polar coordinates in the expansion of ∇^2 ; and there are four pages in small type working in detail through the Kronig-Penney model of a lattice.

It is impossible in a book of this kind to keep a uniform mathematical level. Thus the calculus of variations, which is hard, comes on page 103, just ten pages before the use of an Argand diagram, which is easy. There does not seem to be much that is wrong, though someone new to the Dirac δ -function might be surprised to see it defined (page 131) by $f(x) = \int f(x) \delta(x-x) dx$. Almost inevitably there is a certain inelegance when so much ground has to be covered (for example, the proof of the Uncertainty Principle on page 158).

On the good side it must be said that most of the mathematics really is clear, and the diagrams are excellent, so that if a student were to take up this book and work steadily through it, without any doubt he would be able to learn a lot. It would be an excellent book, not so much for class use, but as a reference volume to which a student could be referred if he found his class lectures unpalatable. C. A. COULSON

Ornithological Statistics

The Visible Migration of Birds at Ottenby, Sweden. Edited by Carl Edeltam. Drawings by Harald Wiberg. Pp. 360. (Swedish Ornithological Association: Stockholm, 1972.) 95 Sw. cr.

THIS is an extraordinary book in several senses of the word. Teams at many bird observatories have counted the birds daily migrating past. In the few cases where analyses have been published it is usually stated that the original data have been deposited at some institute. The Ottenby team decided that this was not good enough and have deposited the original data in the reader's lap. Interpretation and commentary occupy less than a fifth of the book—a tenth, really, since each page is half English, half Swedish.

The data concern ten years, 1947 to 1956, June to October, and 1,509 observation days. The yearly totals for sixty species are presented in the form of histograms elegantly spaced over ten pages. These are then re-sorted into a further set of 10-day period histograms. Then the daily totals for each species

for each year are set out, again as histograms, over 180 pages. The monotony of page (36×22.5 cm) after page of black bars and white space is offset by an elegant line drawing of each species.

Next the hourly variations within each 10-day period are presented in the form of two seven-step ladders, on the rungs of which the histograms are mounted. The extravagance of the layout is even more apparent here, for in half the 70 species given a page apiece, the left or right hand ladder is completely empty.

The production is impeccable, the paper quality high, the draughtsmanship superb, the amount of work appalling. Yet what does it achieve? Certainly, as pointed out in the commentaries, impressions can be gained by visual inspection, but to test them recourse to the original numerical data is still needed. These could be extracted by measurement (the histograms are meticulously accurate) but it would have been simpler (and not much duller) to have the numbers themselves, and to use histograms to illustrate particular points that statistical analysis had shown to be valid.

There is little doubt that this book will remain unique. A wide sale cannot be forecast. G. V. T. MATTHEWS

Geometrical Optics

The Optics of Rays, Wavefronts and Caustics. By O. N. Stavroudis. Pp. xvi+313. (Academic: New York and London, October 1972.) \$18.

THIS interesting and unusual book on geometrical optics begins (after an historical introduction) by obtaining the concept of a ray path in a medium of continuously varying refractive index via the calculus of variations, and continues with an account of the differential geometry of curvature and torsion of generalized space curves. Then the Hilbert integral is defined and used to deduce the mathematical concepts of the wavefront as a transversal of a two-parameter family of rays and the caustic as the envelope of such a family. Snell's law is then derived for a medium of sectionally-continuous refractive index.

Contact with the bread-and-butter of geometrical optics is made in a discussion of ray tracing, but the treatment is at an esoteric level with no real mention of how to do ray tracing in cases of practical interest. It is probably fair to assume, however, that no neophyte in need of such advice would buy the book anyway.

Chapter seven establishes the general condition for the existence of a wavefront to a set of rays and Malus's theorem is formally proved. The chapter on "Generalized Raytracing" concerns the propagation of an element of wavefront through a system and represents, in effect, a generalized paraxial

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ray trace in which the optical axis is replaced by a skew finite ray.

The discussion on classical aberration theory includes Hamilton's characteristic function, Hertzberger's diappoint theory, and an incomplete account of the Seidel aberrations. This is preceded by a partially successful attempt to produce the reverse of the well-known Luneburg derivation of the fundamental properties of geometrical optics from Maxwell's equations.

A radically different mechanism of image analysis is then studied in the form of Hertzberger's fundamental optical invariant and its scalar form the lens equation. This is a system of first-order partial differential equations involving ray coordinates and directions at the object and image planes. The book closes with a closely-reasoned but slightly tongue-in-cheek application of algebraic group theory to lenses—heady stuff for lens designers.

In summary, there is little in the book to cause the designer to rush to the coding sheet to rewrite his programs—it is not a book of that level. But for those of us who enjoy an occasional dip into the rigours of Luneburg there is much here to interest and stimulate, and the author succeeds in guiding us through the welter of mathematics with an entertaining and readable style. JOHN MACDONALD

CORRESPONDENCE

Misidentification or Misunderstanding?

SIR,—The article 'Misidentified Dyke' (*Nature*, 244, 485; 1973) by your geomagnetism correspondent contains the following inaccuracies. (1) The trend of the Wackerfield Dyke is ENE not WNW (Fig. 1). It is important because dyke trends in Northern England have long been recognised as reliable indications of age, WNW for Tertiary and ENE for late Carboniferous (called Carboniferous-Permian before the advent of radiometric age determination). (2) It is not therefore "fairly obvious from field relations that it forms part of the Cleveland-Armathwaite Dyke"; their outcrops are near but their trends are different. The original statement by Tarling *et al.*¹ that "its field relations suggest that it could be part of

the Cleveland-Armathwaite Dyke" is only slightly less misleading. (3) Tarling *et al.* do not claim that the dyke has "always been regarded as part of the Tertiary activity", nor do I know of a publication which does. On the contrary it is unequivocally grouped with the dykes associated with the Upper Carboniferous Whin Sill and equally unequivocally differentiated from the Tertiary Cleveland Dyke in the standard petrographic studies of Holmes and Smith² and Holmes and Harwood³—both quoted by Tarling *et al.* It is also clearly shown as of 'Carboniferous-Permian' age on the Geological Survey one-inch map (Sheet 32: Barnard Castle) published in 1969.

The work of Tarling *et al.* thus con-

firms "long cherished beliefs" rather than requires that they should be discarded. In case it is overlooked, it may be as well to emphasise the real contribution made by Tarling *et al.*—namely the relevance of palaeomagnetic studies in establishing the age of emplacement and subsequent history of intrusions like the Wackerfield Dyke.

Yours faithfully,

D. A. C. MILLS

*Institute of Geological Sciences,
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¹ Tarling, D. H., and Mitchell, J. G., *Earth planet. Sci. Lett.*, 18, 427 (1973).

² Holmes, A., and Smith, S., *Geol. Mag.*, 58, 440 (1921).

³ Holmes, A., and Harwood, H. F., *Mineralog. Mag.*, 21, 493 (1928).

Our Geomagnetism Correspondent writes:

Dr Mills is quite right; I have misunderstood. I measured the trend of the Wackerfield Dyke from the Tarling *et al.* map which, because of its small scale, led to the ambiguity now resolved by Dr Mills' larger scale version. Once this point is cleared up, and accepting the points made by Dr Mills in (3) above, it becomes difficult to understand why Tarling *et al.* should say that "its (the Wackerfield Dyke's) field relationships suggest it could be related to the Eocene Mull Dyke Swarm"—a misleading statement which, compounded by my error in the trend, I am guilty of accepting rather too uncritically.

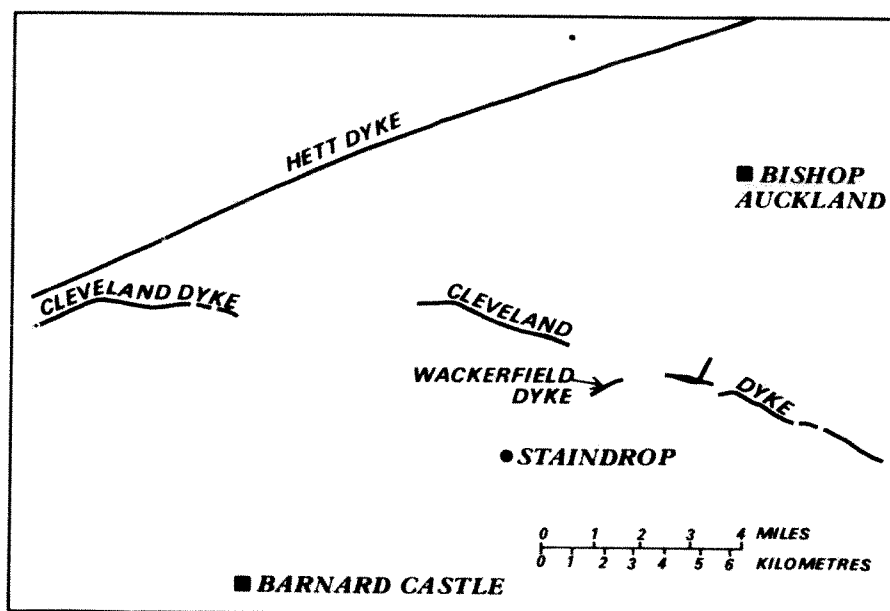


Fig. 1 Map of southern part of Co. Durham showing outcrops of the Hett, Wackerfield and Cleveland Dykes.

Obituary

Professor Jean Hanson

Professor Emmeline Jean Hanson, FRS, Director of the Medical Research Council's Muscle Biophysics Unit at King's College London, died on August 10 of an acute meningococcal infection, at the age of 53.

An only child, she was born in Derbyshire, and was educated at the High School for Girls, Burton-on-Trent, and

at Bedford College in the University of London. After taking her BSc in Zoology, she was engaged in cancer research for two years at the Strangeways Research Laboratory, Cambridge, producing two papers on the histogenesis and differentiation of the mammalian epidermis. She then returned to Bedford College in 1944 with a teaching appointment in the Zoology Department, making a number of histological

and other investigations on several aspects of structure and function in annelids.

The decisive step in her scientific career was her appointment in 1948 to the Biophysics Research Unit, established by the Medical Research Council in the previous year under Sir John Randall, then Wheatstone Professor of Physics at King's College London. She and Randall were put in touch by

Munro Fox, the Head of her Department at Bedford College, and the appointment was as significant for the unit as it was for her. Her wide knowledge of biology was an important factor in a unit where other members had almost all been trained in the physical sciences, and her personal qualities—her energy, her integrity and her helpfulness to others—contributed greatly to the successful development of the unit. The investigations on muscle, which later became one of the chief interests of the unit, were centred on her from the beginning. For the first few years she was the only member of the unit working on muscle, but under her inspiration this side of the unit's activity expanded so that, when the unit was divided after Randall's retirement in 1970, one part became the Muscle Biophysics Unit, and she was appointed as its Director.

Although she held a full-time research appointment, she devoted a large part of her energy to undergraduate teaching at King's College. Not only did she develop courses in Biophysics, both within King's and as part of the inter-collegiate teaching of London University, but she played a key part in the development of the School of Biological Sciences at King's. She often acted as an external examiner, both for undergraduate examinations and for doctoral theses, and made a reputation for sympathetic and conscientious work in this capacity. In 1966, the University of London conferred on her the title of Professor of Biology.

From the time when she first joined Randall's Biophysics Research Unit, almost all of her research was concerned with the structural basis of muscular contraction, and it is for this that she will chiefly be remembered. Her first

attempts at elucidating the changes in the striation pattern during contraction, published in 1952, showed the formation of contraction bands but threw no light on the earlier stages of shortening. Her method, however—observing separated myofibrils under a phase-contrast microscope—was used again by her with great success in a period of highly fruitful collaboration with Dr H. E. Huxley. This began in 1953–54, when both of them spent the year in the laboratory of Professor F. O. Schmitt at the Massachusetts Institute of Technology, she as a Fellow of the Rockefeller Foundation. They first established the localisation of myosin and actin in the striation pattern (also done independently at the same time by W. Hasselbach in H. H. Weber's laboratory) and soon afterwards showed the constancy of the distances in the striation pattern corresponding to the lengths of the thick and thin filaments. This was paralleled in part by A. F. Huxley and R. Niedergerke's measurements on living fibres. Together with H. E. Huxley's evidence from electron microscopy and X-ray diffraction, these results formed the chief basis of the sliding filament theory, now universally accepted.

Her later work, much of it in collaboration with Professor J. Lowy, was almost all carried out with the electron microscope. Most of it was related to two problems: the structure of muscles of molluscs and other invertebrates, and the structure of the thin filaments. Hanson and Lowy were the first to obtain isolated thin filaments, and these showed clearly the helical arrangement of the actin monomers. Later work, on which she was still engaged at the time of her death, was concerned with the position of other components of the thin fila-

ments, tropomyosin and troponin.

Aside from her own investigations, she played a very great part by inspiring the muscle team that she gradually built up. Her name appeared on papers only when she had actually taken a major part in the experimental work, but all the other work from the unit, whether electron microscopy, X-ray diffraction or protein chemistry, owed a tremendous amount to her interest, encouragement and criticism, and to her wide knowledge both of the muscle field and of biology in general. Under the influence of her personality, the unit became an exceptionally happy place, where there was excellent cooperation between the members, and where visitors were made welcome.

She was elected to the Royal Society in 1967. She was outstandingly friendly and helpful towards everyone she had to do with, and will be deeply missed by a wide circle of scientific colleagues and other friends. She was unmarried.

Announcements

University News

Professor C. Michael has been appointed to the chair of theoretical physics, **University of Liverpool**.

Dr J. T. Owen has been appointed to the chair of anatomy, **University of Newcastle upon Tyne**. **Professor A. Mitchell** has been appointed to the William Cochrane Chair of Metallurgy and Engineering Materials, **University of Newcastle upon Tyne**.

Professor W. Williams has been appointed Professor of Agricultural Botany, **University of Reading**.

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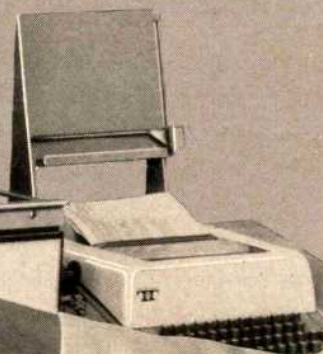
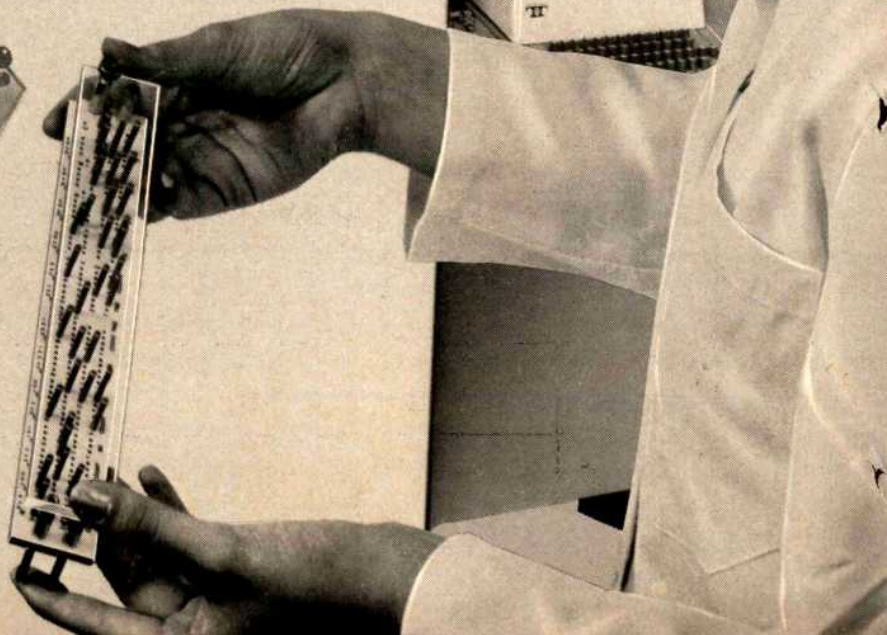
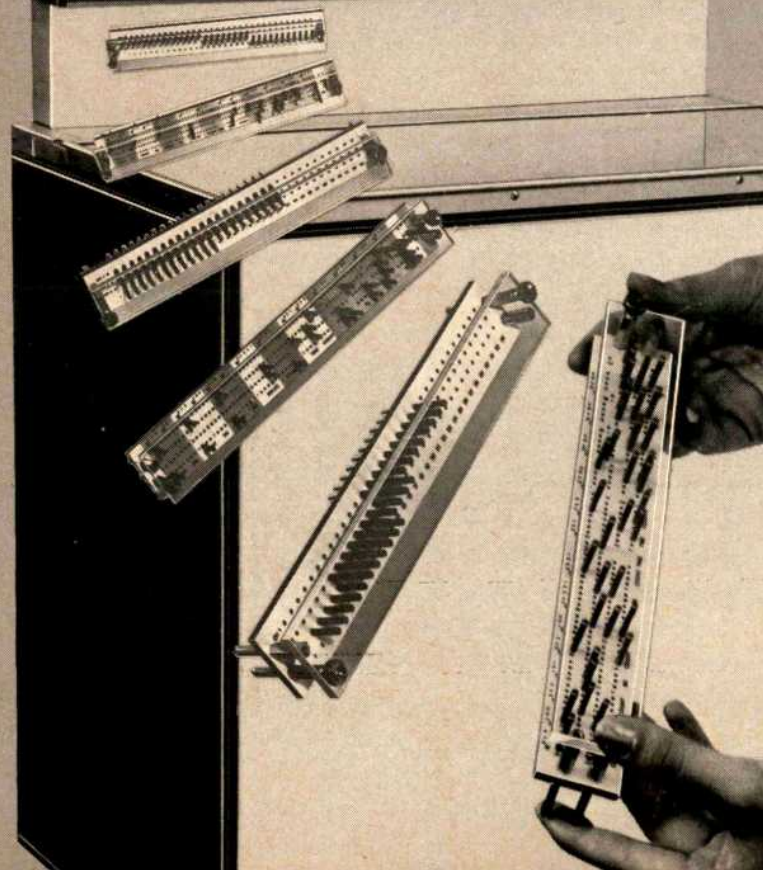
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The post described is partly financed by Britain's programme of aid to the developing countries administered by the Overseas Development Administration of the Foreign and Commonwealth Office.

For further particulars you should apply, giving brief details of experience to:

crown agents

M Division, 4 Millbank, London SW1P 3JD, quoting reference number M3F/730804/NF

(1391)

THE BRITISH COUNCIL SOIL MICROBIOLOGY

A LECTURER is required at the UNIVERSITY OF CEYLON, PERADENIYA, SRI LANKA by January 1974 or as soon after as possible to lecture to students reading for a first degree. Candidates should be citizens of and normally resident in UK, have a PhD from a university in Britain and have relevant teaching experience.

SALARY: £2,714-£4,710 per annum according to experience. Married overseas allowance £770-£97 according to family circumstances. The usual allowances and benefits will be granted including accommodation, travel and children's allowances. One or two-year contract. 73 OU 43

Write quoting relevant reference number to THE BRITISH COUNCIL (APPOINTMENTS), 29 BRESSENDEN PLACE, LONDON SW1E 5DD for further particulars and application form to be completed as soon as possible.

(1365)

ARCHIFAR A Pharmaceutical Industry

has a vacancy at the new Research Laboratories in Northern Italy for a

MICROBIOLOGIST

He will be engaged in research on ANTIBIOTICS and ENZYMES. Applicants must have at least 4 years of post-graduate experience in the field. Applications which should include comprehensive curriculum vitae and addresses of two referees, should be sent to:

Archifar S.p.A., Via Trivulzio, 18, 20146 Milan, Italy.

(1387)



Senior Physicists step into space

Our involvement in a major space project, requires the leadership of a man who can bring heavyweight experience and effort in the field of physics. Following the launch of two highly successful Infra Red Temperature Sounding Radiometers in 1970 and 1972, we are responsible for the Stratospheric Sounding Radiometer of Tiros 'N', the first of a series of fully operational meteorological data gathering satellites. If you are interested and have a good honours degree in physics, possibly a higher degree, tempered by about 5 years' research and development experience in most of the following: Radiometry, Optics, Infra Red Detection, High Vacuum or Thermodynamics we would like to hear from you. At the same time, Physicists with less experience would be considered for a variety of other openings in this pioneering work. Salaries are negotiable and assistance with re-location expenses will be given where appropriate. Write giving comprehensive career details to John Fell, of our Advanced Projects Group, Marconi Space and Defence Systems Limited, Chobham Road, Frimley, Camberley, Surrey. Or telephone Camberley 63311. Ext. 206.

Marconi Space & Defence Systems

A GEC-Marconi Electronics Company

(1457)

UNIVERSITY OF KHARTOUM SUDAN

Applications are invited for post of PROFESSOR/ SENIOR LECTURER/LECTURER IN ENGINEERING MATHEMATICS in the Department of Engineering Mathematics, Faculty of Engineering and Architecture. Salary scales: Professor £53,600 per annum, Senior Lecturer £52,400 to £52,800 per annum, Lecturer £51,500 to £52,300 per annum. The British Government may supplement salary in range £1,300 to £1,800 per annum (sterling) for married appointee or £800 to £1,000 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. Family passages: various allowances; superannuation scheme; annual overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail not later than November 29, 1973, to the Personnel Secretary, University of Khartoum, P.O. Box 321, Khartoum, Sudan. Applicants resident in U.K. should also send one copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars are available from either address. (1360)

UNIVERSITY OF WINDSOR WINDSOR, ONTARIO, CANADA

Applications are invited for:

HEAD DEPARTMENT OF BIOLOGY

Applicants are expected to have a distinguished record in research and teaching. Duties include: administration of a sixteen member department which offers undergraduate and graduate courses (through doctoral level) in a broad spectrum of biological sciences; fostering the development of research programmes; and participation in research and teaching.

The appointment commences July 1, 1974. Salary to be negotiated according to qualifications and experience.

Please send application, curriculum vitae, names of at least three referees and other pertinent information to:

Chairman of Selection Committee,
Department of Biology,
University of Windsor,
Windsor, Ontario, Canada.

(1310)

UNIVERSITY OF MANCHESTER LECTURER IN VIROLOGY

Applications invited for this post from candidates with or without medical qualifications. Salary ranges per annum: (clinical) £2,535 to £5,361; (non-clinical) £1,929 to £4,548. F.S.S.U.

Further particulars and application forms (returnable by November 30) from the Registrar, The University, Manchester M13 9PL. Quote Ref. 191/73/Na. (1351)

CHAIRMAN—DEPARTMENT OF ANATOMY

Columbia University, College of Physicians and Surgeons, an equal opportunity employer, is seeking an individual as Chairman of Anatomy Department. Should be qualified medical scientist and experienced medical educator.

Send curriculum vitae to: Myron Winick, M.D., Chairman, Search Committee, Institute of Human Nutrition, 511 West 166th Street, New York, New York 10032. (1289)

UNIVERSITY OF LONDON KING'S COLLEGE

LECTURER IN PLANT SCIENCES

Applications are invited for the post of Lecturer in Plant Sciences, tenable from April 1, 1974, or as soon after as possible. Applicants must have a good Honours degree, and an interest in phytochemistry and its application to systematic and/or ecological problems would be an advantage. Salary scale £1,929 to £4,548 plus £162 London Allowance (starting salary according to qualifications and experience). F.S.S.U. pension scheme.

Application forms and conditions of appointment may be obtained from the Registrar (N), King's College, Strand, London WC2R 2LS, and must be received by November 23, 1973. (1358)

UNIVERSITY OF GLASGOW S.R.C. RESEARCH ASSISTANTSHIP IN POLYMER CHEMISTRY

A vacancy exists for a Research Assistant in Polymer Chemistry, a post financed by S.R.C. through funds available to the Glasgow Polymer Centre. The appointment (which may commence at any time up to January 1, 1974) is initially for one year, with the possibility of extension for a further two years. The salary will be in the region of £1,900 to £2,000 plus F.S.S.U. The person appointed would be expected to carry out research work in the field of degradation of polymer blends or of block or graft copolymers, and might be asked to make a minor contribution to the teaching of the Department.

Applicants should send full details of their qualifications (for which the minimum requirement is a Ph.D. degree or its equivalent) and research experience, together with the names of two referees, to Professor N. Grassie, Chemistry Department, University of Glasgow, Glasgow G12 8QQ, Scotland. In reply please quote Ref. No. 3375. (1370)

RESEARCH TECHNICIAN

required for English-speaking molecular biology department in modern research institute involved in study of viral transformation of animal cells in culture. Experience with general biochemical techniques in enzymology and subcellular fractionation and with general sterile techniques associated with tissue culture useful. Salary on BAT scale from DM14,600 to DM17,880 per annum, according to experience, plus family allowances.

Applications, with the names of two professional referees, should be sent to Dr. D. Jovin, Abt. Molekulare Biologie, Max Planck-Institut für Biophysikalische Chemie, 34-Göttingen-Nikolausberg, POB 968, W. Germany. (1297)

UNIVERSITY OF SURREY DEPARTMENT OF BIOCHEMISTRY

A vacancy occurs for a LECTURER with an interest in molecular aspects of pharmacology to participate in the teaching of pharmacology and biochemical pharmacology in the undergraduate and postgraduate courses in biochemistry, nutrition, toxicology and other medical sciences.

The candidate, who may be a graduate of biochemistry, pharmacology or medicine, will be expected to participate actively in research and in liaison with industry. Appropriate research and industrial experience will be considered advantageous.

Salary will be on the scale £1,929 to £4,548 with F.S.S.U. provision.

Further particulars may be obtained from the Academic Registrar (LFG), University of Surrey, Guildford GU2 5XH, telephone Guildford 71281, extension 452. Applications, in the form of a curriculum vitae, together with the names and addresses of two referees, should be sent to the same address by Monday, December 3, 1973. (1376)

Centre for Overseas Pest Research

Deputy Director £6982-£7825

The Centre is a research, training and technical assistance unit concerned with pests of international or regional significance. Its main fields are pre-harvest pest and vector control in agriculture and public health in developing countries. Employing 150 people—90 of whom are qualified scientists—it carries out biological, ecological and control systems research, working closely with relevant organisations at home and overseas in the application of this knowledge to develop practical pest management systems.

The Deputy Director will be responsible for the day-to-day running of the Centre and will be involved with major policy formulation, in liaison with other O.D.A. departments, U.N. agencies, international organisations

and overseas governments. There will be extensive travel abroad.

Candidates must have a 1st or 2nd class honours degree in an appropriate subject and research experience, backed by considerable relevant practical and administrative experience.

Starting salary will be within the quoted scale.

Non-contributory pension scheme.

Fuller details of this appointment may be obtained by writing to the **Civil Service Commission, Alencon Link, Basingstoke, Hants., RG21 1JB**, or by telephoning **BASINGSTOKE 29222 ext. 500** or **LONDON 01-839 1992** (24-hour answering service), quoting **S/8421/U**. Closing date **31 December 1973**.

Overseas Development Administration

(1452)

McMASTER UNIVERSITY VIROLOGIST

A position is available for a Virologist at the Assistant or Associate Professor level. The appointee will be part of a viral oncology group being formed at McMaster University as well as a member of the Department of Biology. His/her research interests should be the molecular biology and/or genetics of animal viruses. His/her primary responsibility will be research and supervision of graduate students.

Applicants should send their curricula vitae and the names of three referees to the Chairman, Department of Biology, McMaster University, Hamilton, Ontario L8S 4K1, Canada, to arrive no later than January 15, 1974. (1381)

A NEW MEDICAL SCHOOL AT MEMORIAL UNIVERSITY OF NEWFOUNDLAND, ST. JOHN'S, NEWFOUNDLAND, CANADA

is expanding its faculty and is now ready to make appointments in the field of cell sciences. New buildings to house the cell sciences research group, which is part of the larger division of cell studies, will be ready for occupancy by 1975. The health sciences complex now under construction is a medical school with extensive research areas plus a biomedical library and 400-bed hospital.

Applications are now invited for a senior level position who would be able to organize a research team and participate in the inter-disciplinary teaching of medical students.

Interested individuals should submit applications, accompanied by a detailed curriculum vitae, to Professor B. H. Sells, Ph.D., Chairman, Search Committee, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland, Canada. (1382)

CHELSEA COLLEGE UNIVERSITY OF LONDON

TECHNICIAN GRADE 2B required for teaching laboratories dealing with the extraction of materials of medical importance from plants. Good working conditions. Salary scale £1,699 to £1,969 (including London Allowance).

Application forms from Manager of Technical Services (N), Department of Pharmacy, Chelsea College, Manresa Road, London SW3 6LX. (1392)

EAST MALLING RESEARCH STATION ASSISTANT STATISTICIAN

The Computing Unit requires an Assistant Statistician to undertake the processing of data from agricultural experiments.

The minimum qualification is a degree, H.N.C. or equivalent in a relevant discipline.

The appointment will be in the grade of Scientific Officer (£1,318 to £2,177), starting salary depending on qualifications and experience. It will be for three years, but may be extended.

Application forms and further details from the Assistant to the Secretary, East Malling Research Station, East Malling, Maidstone, Kent. (1393)

NATURE CONSERVANCY COUNCIL

Design and exhibition opportunities

There are 2 posts at Attingham Park, near Shrewsbury, within a small team concerned with publication, displays and other interpretative work.

The duties of the first post will include advising on design, illustration and layout, contracting out and supervising the execution of specific projects. Candidates must have an up-to-date knowledge of design precepts and techniques, and of sources of material and services. Experience in photographic and audiovisual techniques and some knowledge of natural history would be advantageous.

The second post is concerned with organising the exhibitions programme, selecting material, contracting out and supervising projects, arranging storage, distribution and maintenance of displays. Relevant experience is essential; an appropriate qualification and some knowledge of natural history desirable.

Starting salary may be above the minimum of the scale £2445-£2961. Promotion prospects: Non-contributory pension scheme.

For full details and an application form (to be returned by 21 November 1973) write, quoting **G(14)/634**, to the Civil Service Commission, Alencon Link, Basingstoke, Hants, RG21 1JB, or telephone Basingstoke 29222 ext. 500 or London 01-839 1992 (24 hour answering service).

(1354)

THE MEDICAL COLLEGE OF ST. BARTHOLOMEW'S HOSPITAL WEST SMITHFIELD, EC1A 7BE

Applications are invited for three posts of **LECTURER IN PHYSIOLOGY**, tenable from January 1, 1974. Salary scale £1,929 to £4,548 per annum, plus £162 London Allowance and membership of the F.S.S.U.

Forms of application may be obtained from the Secretary of the Medical College, and should be returned to the Dean not later than November 30, 1973. Further particulars may be obtained from the Department of Physiology. (1384)

ROYAL HOSPITAL FOR SICK CHILDREN

GRADUATE AS TECHNICIAN to join a group involved in the diagnosis and investigation of inborn errors of metabolism. The appointee would be responsible for lysosomal enzyme assays on cultured and uncultured cells. Previous experience not essential as full training will be given. Salary scale £1,390 to £2,292.

Applications, in writing, together with names and addresses of two referees, to the Secretary, Royal Hospital for Sick Children, 1 Rillbank Terrace, Edinburgh EH9 1LN. (1364)

ITALY

Important Italian Chemical Pharmaceutical Industry, with headquarters in Milano, operating at international level, seek

Head of Chemical Research

The successful candidate will work in the Research Department, will be an organic chemist, experienced in medicinal chemistry, creative-minded and with organisation capabilities.

His responsibilities will involve:

planning and directing the research of a team of experienced organic chemists for the scope of designing and synthesizing new therapeutically active molecules.

co-ordinating chemical research with pharmaco-biological screening of the new substances.

The position offers the candidate the possibility to develop his scientific personality within a Company that are leaders in pharmaceutical research. Knowledge of Italian would be an advantage.

Salary according to qualifications and in any case attractive.

Please send detailed curriculum vitae and salary requirements (for further transmission to the advertiser) first to:

SE/6647 Advertising Agency Dr Giuliano Blei, 8 Piazza del Liberty, I-20148 Milano (Italy).

(1407)

The United Sheffield Hospitals

A vacancy exists, for a period of 3 years, in the Transplantation Unit and Department of Urology, Royal Hospital, Sheffield, for a

Non-Medical Scientific Officer

to take part in a current experimental study into Transplantation of Islets of Langerhans in animals with a view to treating Diabetes. The work offers new avenues in the possible management of this condition.

Candidates should possess a 1st or 2nd class Honours degree in an appropriate subject (e.g., Zoology, Biochemistry, Physiology, Biology). The research offers an opportunity for acquiring a higher qualification. Whitley Council Conditions of Service apply. Salary Scale £1,566-£1,980 p.a.

Applications, stating age, qualifications and experience and naming two referees to: The Acting Chief Administrative Officer, United Sheffield Hospitals, 10 Beech Hill Road, Sheffield S10 2RZ, by 17th November, 1973. Further details supplied on request.

(1418)

UNIVERSITY OF MANCHESTER DEPARTMENT OF ZOOLOGY RESEARCH ASSISTANT IN CYTOLOGY

Applications invited for this post (funded by the O.D.A.) for research connected with tsetse fly and trypanosome control, involving the investigation of DNA/RNA synthesis during gametogenesis, oogenesis and vitellogenesis, and the cytogenetics of species, hybrids and radiation induced mutants. Post tenable until September 30, 1976, with an initial salary up to £2,058 per annum rising to £2,388 per annum. F.S.S.U.

Detailed applications, with names of two referees, should be sent to Dr. D. I. Southern, Department of Zoology, The University, Manchester M13 9PL, as soon as possible. (1404)

CHARING CROSS HOSPITAL (FULHAM)

FULHAM PALACE ROAD, HAMMERSMITH W6
DEPARTMENT OF MEDICAL ONCOLOGY

GRADUATE BIOCHEMIST required as part of a team isolating tumour antigens for immunodiagnosis. Experience in protein chemistry, immunochemistry, or in tissue culture work required. Suitable candidates have opportunity for Doctorate studies.

Salary on scale £1,404 to £2,496 (inclusive of London Weighting) according to qualifications and experience.

Please send curriculum vitae, with names and addresses of two referees, to Miss Matthews, Personnel Department, quoting Ref. 963, by November 9. (1375)

WEED RESEARCH ORGANIZATION Begbroke Hill, Yarnton, Oxford OX5 1PF

The Agricultural Research Council require a SCIENTIFIC OFFICER or HIGHER SCIENTIFIC OFFICER for a NEW POST in the Information Department of the Weed Research Organization (WRO) near Oxford. Duties include provision of scientific secretarial and editorial services associated with the varied commitments of the institute. Notably, help is given to the British Crop Protection Council in the organization of the scientific programmes of weed control conferences and technical symposia and in the compilation and editing of the Weed Control Handbook and other publications.

Within WRO the officer will serve as scientific secretary to committees responsible for the planning and co-ordination of the research programme. Assistance is also required in editing WRO publications and undertaking a variety of other information activities.

QUALIFICATIONS: Science degree or equivalent and interest in agriculture, with experience in scientific writing and the administration of technical committees. Ability to drive a car essential.

SALARY: Scientific Officer Scale (£1,318-£2,177 p.a.) or Higher Scientific Officer Scale (£2,076-£2,667 p.a.) depending on qualifications and experience, a minimum of five years' post-qualifying experience being required for appointment in the higher grade.

The post is superannuated with contributions off-set by a non-pensionable allowance of 5½ per cent of gross salary.

Application forms and further particulars available from Secretary, Weed Research Organization, Begbroke Hill, Yarnton, Oxford OX5 1PF. Telephone Kidlington 3761. Closing date for applications November 30, 1973. (1394)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS AL5 2JQ

SCIENTIFIC OFFICER to assist with the study of soil minerals by physico-chemical methods including spectrometric analysis and X-ray diffraction. Minimum qualifications: pass degree, H.N.C. or the equivalent in chemistry. Starting salary £1,318 to £1,590 according to qualifications and experience on a scale to £2,177. Superannuation with allowance to offset contributions.

Applications, naming two referees and quoting Reference 2002, to the Secretary by November 30, 1973. (1397)

UNIVERSITY OF THE SOUTH PACIFIC—SCHOOL OF NATURAL RESOURCES

Applications are invited for the post of LECTURER IN BIOLOGY in the School of Natural Resources at the University of the South Pacific for appointment early in 1974. The vacancy is for a Population Ecologist. Preference will be given to an applicant with a Ph.D. and whose main interests are with either Microbial or Vertebrate Populations. The successful applicant will be required to conduct lectures, laboratories and tutorials at all levels of the degree programme and will be encouraged to contribute to advanced teaching and research within his own area of specialisation.

Salary in scale \$F4,700 to \$F200 to \$F6,300 (Lecturer scale) placing in accordance with qualifications and experience. Note: this salary scale is under review. (£1 sterling=\$F1.88.) 10 per cent annual gratuity for contract appointment, superannuation contributions, partly furnished accommodation at rental of 15 per cent of salary, appointment allowance. Contracts may be for two, four or six years.

Details of form of application, further particulars, and outline of terms of service are available from the Registrar (Post 73/50), University of the South Pacific, P.O. Box 1168, Suva, Fiji, to whom completed applications (6 copies) should be returned by November 16, 1973. (1401)

QUEEN MARY COLLEGE UNIVERSITY OF LONDON DEPARTMENT OF PHYSICS

Applications are invited for a Postdoctoral Research Associateship to work with Dr. P. E. Clegg on the design, construction and operation of a beam-switching, submillimetre astronomical detector for use on a variety of large telescopes.

Candidates should have a Ph.D. in physics or electronic engineering and experience in infrared photometry or spectroscopy, and preferably also in electronics.

Appointment will be initially for one year, to begin as soon as possible. Salary within range £2,388 to £3,048 per annum, plus £162 London Allowance.

Applications (giving age, qualifications, experience, and names and addresses of two referees) to the Registrar (N), Queen Mary College, Mile End Road, London E1 4NS, as soon as possible. (1402)

JUNIOR TECHNICIAN REQUIRED IN THE Department of Medicine to assist with research. Salary according to age and qualifications.—Apply in writing to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, quoting Ref. D.M.1. (1390)

New Influenza Vaccines

Virologist

from £3000

This is an opportunity for a graduate with good experience of virology or vaccine work to play a prominent role in a project concerned with new influenza vaccine research.

The scope of the work spans a wide range of activities from pure research to vaccine development, including the preparation and assay of new virus strains, and the development of new techniques for the culture, purification, concentration and preservation of viruses. To help him in this, he will have two people reporting to him. The work will also involve interdisciplinary cooperation with clinical researchers, production staff and other research and development teams.

The man (or woman) we seek for this key appointment will be aged up to about 35, and will have good research experience in virology or bacterial vaccine work. He should have an applied interest in viruses *per se*, rather than an academic interest in viruses as a research tool.

Particularly advantageous would be familiarity with vaccine work, experience of handling viral cultures on a development scale, practical expertise in biophysical techniques used for purification and preservation, and/or experience of animal experimentation.

Our client is a large and well-known company with extensive interests in chemotherapy and the life sciences, and the position has arisen due to the recent promotion within the Company of the senior scientist previously involved in these studies.

Starting salary for this appointment is likely to be at least £3000, and substantially higher for a particularly suitable candidate. Other benefits include a bonus scheme, free life assurance, generous pension scheme, a pleasant geographical location in Southern England in a lowish cost housing area, and extensive financial assistance towards removal and re-establishment costs.

Please write for an application form, or phone if you would like to discuss the position further:

A. E. F. Chandler, M.A., Ph.D., D.I.C., M.I. Biol.,
Talentmark Limited,
King House,
5/11 Westbourne Grove,
London W2 4UA.
Tel: 01-229 2266.

(1441)



Talentmark
Biomedical and Scientific Consultants

THE EDINBURGH SCHOOL OF AGRICULTURE RESEARCH ASSISTANT

Applications are invited for a post of Research Assistant to be employed on an investigation of vernalisation of the seedlings of biennial brassica crops and growth at low temperatures. Candidates should have a good honours degree in Botany or Agricultural Botany and will be expected to register for a higher degree.

Salary scale £830 by £40 to £910. F.S.S.U. Further particulars and application form from the Secretary, The Edinburgh School of Agriculture, West Mains Road, Edinburgh EH9 3JG. (1410)

UNIVERSITY OF EDINBURGH DEPARTMENT OF PHYSIOLOGY LECTURER

The University Court invites applications for a post of Lecturer in the Department of Physiology from January 1, 1974. Applicants must have a good Honours degree in Physiology or a related subject, and a Ph.D. or equivalent research experience. The salary scale for Lecturers is: £1,929 by £129 to £2,058 by £165 to £4,368 by £180 to £4,548. Membership of F.S.S.U. is required.

Applications (6 copies), including the names of at least two referees, should be submitted not later than November 17, 1973, to the Secretary to the University, Old College, South Bridge, Edinburgh EH8 9YJ, from whom further particulars may be obtained. Please quote Reference 1064. (1409)

MEDICAL RESEARCH COUNCIL RHEUMATISM UNIT

CANADIAN RED CROSS MEMORIAL HOSPITAL
TAPLOW, MAIDENHEAD, BERKS

A graduate research assistant (JUNIOR TECHNICAL OFFICER) is required to work in the field of lysosomal physiopathology in arthritis at the above unit. Some previous experience and interest in cellular physiology or biochemistry is desirable.

Applications, with names of two referees, to the



Wellcome

Graduate Scientists

A Chance to Change Direction

The Wellcome Foundation is a rapidly expanding international pharmaceutical organisation.

A vital link between our R & D activities and the world-wide distribution of medical products by the companies of the Wellcome group is the product registration department based at its London headquarters. Most countries of the world require new medical products to be registered for sale before marketing starts and this work is the responsibility of this department. It involves intelligent use of R & D reports and commercial and other information to meet the varied requirements of registration.

We are looking for a graduate chemist, pharmacist or biological scientist, probably aged 25-35, to join the department. This is a chance to move away from pure technical work and gain experience in an interesting and important sphere of this group's international activities.

In addition to an attractive salary the group offer excellent conditions of employment including assistance with relocation expenses where appropriate.

Please write giving brief career details to: Group Personnel Division (PB), The Wellcome Foundation Ltd., 183 Euston Road, London NW1 2BP



(445)

HOECHST PHARMACEUTICALS RESEARCH LIMITED

RADIOLOGICAL AND GENERAL SAFETY OFFICER

We require an experienced science graduate to act as Radiation and Safety Officer for the Hoechst Pharmaceutical Research Centre presently nearing completion at Milton Keynes, Bucks.

The work of the laboratories will include the extensive use of radio isotopes to solve biological research problems.

The person appointed will be responsible for all aspects of laboratory safety both conventional and radiological including dosimetry, radiation measurement and contamination control for a variety of nuclides as well as effluent control for the entire centre.

This is a responsible position in a new organisation and facilities are first class.

Salary is negotiable, according to qualifications and experience, and there are excellent company benefits including annual bonus, contributory pension scheme and free membership of Private Patients Plan.

Please write, with full details of career to date, to:

**Mrs. M. Hannay, Personnel Officer,
Hoechst UK Limited,
Hoechst House, Salisbury Road,
Hounslow, Middx.
Tel: 01-570 7712**

(1363)



AUTOANALYSIS- FOOD INDUSTRY

Heinz, leaders in the convenience sector of the food industry, require a young graduate, preferably with some experience in continuous flow autoanalysis, to carry out development work on foodstuffs analysis by this technique.

The person appointed must have sufficient experience and initiative to perform this task with minimum supervision.

The Heinz Research Centre is situated in a pleasant parkland setting in Hayes, Middlesex, and assistance in relocation can be offered if necessary. Salary, working conditions and fringe benefits are appropriate to a major food company.

Please write in the first instance giving a brief personal and career summary and quoting present salary to:—

**Mr. K. S. Chivers,
Manager—H.O. Personnel Services,
H. J. Heinz Company Ltd.,
Hayes Park, Hayes,
Middlesex UB4 8AL**

(1367)

L'ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE

met au concours pour son Département d'Electricité un poste de

PROFESSEUR DE MICROELECTRONIQUE A TEMPS PARTIEL

Domaine d'activité: enseignement théorique et expérimental, en particulier sur les techniques de conception et de fabrication de circuits intégrés. Animation d'un laboratoire pour les étudiants. Collaboration avec les professeurs d'autres départements.

Le poste pourra, au besoin, être occupé à plein temps. Il comportera alors la création d'un laboratoire de recherche.

Qualités requises: formation scientifique approfondie, en particulier dans le domaine de la physique appliquée. Expérience pratique de la fabrication de dispositifs à semi-conducteurs, notamment de circuits intégrés. Talent pédagogique reconnu.

Entrée en fonction: à convenir

Les personnes intéressées, de nationalité suisse ou étrangère, sont invitées à demander le dossier relatif à ce poste à la :

DIRECTION DE L'ECOLE POLYTECHNIQUE FEDERALE DE LAUSANNE 33 AV. DE COUR, 1007 LAUSANNE-SUISSE.

(1378)

MICROBIOLOGIST

A Ph.D. Microbiologist with a strong background in genetics and 5-15 years of experience is needed to manage a group of a dozen people involved in Research and Development in the areas of penicillins, cephalosporins and other antimicrobial agents.

Familiarity with mutation techniques, strain development, antibiotic screening and experimental fermentation would be desirable attributes for the position.

WYETH has been a major producer of antibiotics for the past 30 years and is now expanding its Research and Development efforts in this field. The laboratories are located in Chester County, Pa., in the western suburban Philadelphia area.

Please send reasonably detailed résumé to Mr. Charles L. Smith, Research Administrator.

**Wyeth
Laboratories, Inc.**

P.O. Box 8299
Philadelphia, Pa. 19101 U.S.A.

An Equal Opportunity Employer.

(1377)

Editorial Assistant for NATURE

A vacancy has arisen for an editorial assistant in the production department of 'Nature'. The assistant will handle scientific manuscripts from the time they are accepted by the journal until they are published.

This involves proof reading and correcting, communication with authors and collaborating with printers. Although a degree is not a necessary qualification, a good background in science is. Typing skills are also essential.

**Write the Editor, Nature
4 Little Essex Street, London, W.C.2.**

(1449)

THE ANIMAL VIRUS RESEARCH INSTITUTE

PIRBRIGHT, WOKING, SURREY

DEPARTMENT OF EXPERIMENTAL
PATHOLOGY

Applications are invited for a post in the above Department. Applicants should have had experience in histological, histochemical and immunohistological procedures to provide support for a small group studying the pathogenesis of vesicular diseases in farm animals. Familiarity with the preparation of specimens for, and the use of, the electron microscope an advantage. The appointment will be in either the S.O. grade (£1,318 to £2,177) or H.S.O. grade (£2,076 to £2,667), depending on qualifications and experience. Minimum qualifications required: degree in scientific subject, I.M.L.T., H.N.C., H.N.D. or equivalent for appointment in S.O. grade; similar qualifications required for appointment in H.S.O. grade with at least five years' appropriate scientific experience since qualifying; applicants with first or second class honours degrees or equivalent should have had at least two years' post-graduate research experience. Superannuation scheme with allowance to offset contributions. House available for suitable married applicant. Further particulars and application forms from Secretary.

(1398)

SOUTHAMPTON UNIVERSITY HOSPITALS

Royal South Hants Hospital

QUALIFIED TECHNICIAN/ RESEARCH ASSISTANT

required to work with Dr. S. Roath on projects in the field of cell culture and fine structure. Salary for Basic Grade Technician £1,440-£2,292 or Graduate Biochemist £1,278-£1,980 as appropriate.

Further information available from Dr. S. Roath.

Tel.: 559122. Ext. 2128.

Applications giving curriculum vitae and naming two referees should be sent to Personnel Officer, Southampton University Hospitals, 119 Tremona Road, Southampton, SO1 6HU.

Tel.: 777222. Ext. 3002. Closing date November 22nd 1973.

(1405)

SCIENCE MUSEUM

ASSISTANT KEEPER —CHEMISTRY COLLECTIONS

... to be responsible for the development, historical research and the preparation of publications for the Chemistry Collections covering the fields of Pure, Analytical and Industrial Chemistry, and Chemical Engineering.

Candidates should normally have a good honours degree or a post-graduate degree or an equivalent qualification in a branch of Chemistry, Chemical Engineering, Pharmacy or the History of Science. Ability to write lucidly on technical subjects essential.

Salary: Assistant Keeper, First Class, £2,924-£4,788; Assistant Keeper, Second Class, £1,642-£2,620. Level of appointment according to age, qualifications and experience. Starting salary may be above the minima. Non-contributory pension scheme.

For full details and an application form (to be returned by 23 November 1973) write to Civil Service Commission, Alencon Link, Basingstoke, Hants, RG21 1JB, or telephone BASINGSTOKE 29222, ext. 500 or LONDON 01-839 1992 (24 hour answering service), quoting G(43)/382/2.

(1395)

INSTITUTE OF ORTHOPAEDICS

British Postgraduate Medical Federation
University of London

Applications are invited for the post of

BIOCHEMIST (Senior Grade)

in the Department of Biochemistry, Institute of Orthopaedics. The post involves duties in connection with the clinical chemistry service for the Royal National Orthopaedic Hospital and with the laboratory of a Metabolic Unit for the investigation of bone disease. Opportunities for associated research and for studying for a higher qualification. Whitley scale plus London Weighting.

Applications, stating age, qualifications and experience, to Dr. P. G. Walker, Department of Biochemistry, Institute of Orthopaedics, Brockley Hill, Stanmore, Middlesex, from whom further information may be obtained.

(1419)

Department of the Environment
Princes Risborough Laboratory

Analytical Chemist

■ Investigate timber preservation problems ■ Apply routine analytical techniques ■ Adapt and develop research methods.

□ Degree/HNC in Chemistry □ Age under 30 □ Appointment as Scientific Officer (£1318 - £2177) or Higher Scientific Officer (£2076 - £2667). □ Ref: SA/32/HA □ Closing date 23 November 1973.

□ Application forms from Establishments Office, Princes Risborough Laboratory, Princes Risborough, Aylesbury, Bucks. HP17 9PX.

Overseas Development Administration
Centre for Overseas Pest Research, London

Biologist

■ Investigate mode of action of molluscicides in aquatic snails, using scintillation counting and autoradiographic techniques ■ Post tenable until July 1976.

□ 1st/2nd hon's degree □ Experience in methods employed advantageous □ Age under 30 □ Appointment as Higher Scientific Officer (£2251 - £2842) or Scientific Officer (£1493 - £2352) □ Ref: SA/6/JA □ Closing date 23 November 1973.

□ Application forms from Administrative Secretary, Centre for Overseas Pest Research, College House, Wrights Lane, London W8 5SJ.

Overseas Development Administration
Tropical Products Institute, London SW1

Food Biochemist

■ Join multidisciplinary team studying scientific problems in processing primary products ■ Develop new food products in laboratory ■ Independent work in developing countries possible.

□ 1st/2nd hon's degree □ Relevant experience in food processing, including dehydration □ Age under 27 □ Appointment as Scientific Officer (£1493 - £2352) □ Ref: SA/9/JD □ Closing date 23 November 1973.

□ Application forms from Administrative Secretary, Tropical Products Institute, 127 Clerkenwell Road, London EC1R 5DB.

**Science
group
CIVIL SERVICE**

(1444)

INSTITUTE OF PSYCHIATRY DEPARTMENT OF NEUROLOGY POST-DOCTORAL RESEARCH WORKER

Applications are invited from doctorates in biochemistry/pharmacology for the above post in the Section of Biochemistry of the Department of Neurology. The successful applicant will work on the biochemistry of cerebral amines in relation to basal ganglia disease, and there will be the opportunity to pursue their own research interests. Salary scale £1,926 to £2,241, renewable annually up to 3 years. Closing date November 30.

Applications in writing (quoting Reference PJ/N), together with a curriculum vitae, should be sent to the Secretary, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF, from whom further details may be obtained.

Applicants who wish to visit the unit may do so by prior arrangement. Telephone 01-703 5411, Ext. 245. (1359)

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL (UNIVERSITY OF LONDON) DENMARK HILL, LONDON SE5 8RX

Applications are invited for a newly established post of LECTURER (non-medical) in Immunology. Commencing salary in the range £1,929 to £4,548 plus £162 London Allowance, according to age, qualifications and experience.

Applications, in writing, not later than November 19, 1973, to the Secretary of the Medical School (N), from whom further particulars may be obtained. (1362)

RIVERINA COLLEGE OF ADVANCED EDUCATION

Applications are invited for appointment to the following position:

GEOGRAPHER

A general human Geographer is required preferably in the field of population/urban geography.

The appointee would be expected to lead a small group of geographers within the School of Applied Science.

Salary: Lecturer, \$A8,698 to \$A11,982; Senior Lecturer, \$A12,268 to \$A14,308.

Substantial experience in university teaching is essential for appointment at Senior Lecturer level.

Application forms and further information may be obtained from the Bursar, P.O. Box 588, Wagga Wagga, N.S.W. 2650 (phone 25 1026, ext. 7). (1372)

UNIVERSITY OF LONDON READERSHIP IN PHARMACOLOGY AT THE SCHOOL OF PHARMACY

The Senate invite applications for the above Readership from candidates with experience in teaching and research in pharmacology. Salary scale £4,368 to £5,496 a year plus £162 London Allowance.

Applications (10 copies) must be received not later than December 5, 1973, by the Academic Registrar (N), University of London, Senate House, London WC1E 7HU, from whom further particulars may be obtained. (1400)

BIOLOGIST

Applications are invited for a full-time opening in the Cell Biology Division for a well-trained Ph.D. interested in committing his/her efforts to developing organ culture systems to investigate the differentiation and altered differentiation of epithelial tissues in response to vitamin A, vitamin A analogues, and carcinogens.

Should have training and background in organ/tissue culture, a good basic biological training, and be acceptably knowledgeable in biochemistry. A recent Ph.D. or one with one to two years' post-doctoral training would be acceptable.

Please send recent curriculum vitae to:

Personnel Office
Southern Research Institute
2000 Ninth Avenue South,
Birmingham, Alabama 35205, U.S.A.

An Equal Opportunity Employer M/F.

(1389)

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE (UNIVERSITY OF LONDON)

Applications are invited from post-doctoral BIOCHEMISTS experienced in electrophoresis or ENTOMOLOGISTS interested in insecticide resistance in aphids to work with Dr. R. J. Berry on the biochemical detection and maintenance of insecticide resistance in aphids. Salary in the range £1,929 to £2,200, plus F.S.S.U. Benefits. It is hoped to make an appointment as soon as possible, and applications should be submitted before November 21 to Dr. R. J. Berry, Royal Free Hospital School of Medicine, 8 Hunter Street, London WC1N 1BP. (1412)

KINGSTON POLYTECHNIC GRADUATE RESEARCH ASSISTANT

(Salary: £1,427-£1,537)

Honours graduate required to investigate the degradation of plastics by hot water. The project is supervised by Dr. G. Pritchard in the School of Chemical Science and Technology. Candidates should have the capacity to work for a higher degree and be interested in instrumental methods of materials examination.

Apply for forms and particulars as soon as possible to the Appointments Officer, Kingston Polytechnic, Penrhyn Road, Kingston upon Thames KT1 2EE, quoting Ref. GPI. (1414)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS. AL5 2JQ

BIOLOGIST required for Entomology Department for work on the pathology of insects of agricultural importance. Minimum qualifications: pass degree, H.N.C. or equivalent qualification in biological subjects.

Appointment in grade of Scientific Officer; starting salary £1,318 to £1,590 (depending on qualification and experience) on scale to £2,177. Superannuation with allowance to off-set contributions.

Applications, naming two referees and quoting Reference 2032, to the Secretary by November 30, 1973. (1415)

UNIVERSITY OF AUCKLAND NEW ZEALAND

SCHOOL OF MEDICINE

LECTURESHIP IN HAEMATOLOGY

Applications are invited for the above-mentioned post from candidates holding a medical qualification registrable in New Zealand, together with a recognised postgraduate qualification in either pathology or medicine (for example, F.R.C.P.A., M.R.C.Path., M.R.A.C.P., M.R.C.P.). It is envisaged that the successful applicant will have or will develop a special interest in a particular field of haematology.

Commencing salary will be established in accordance with qualifications and experience. The present salary scale for a medically qualified Lecturer is \$NZ8,931-\$NZ10,551 (bar)-\$NZ12,762 per annum. Lecturers appointed above the bar may be paid an allowance of up to five per cent for clinical responsibilities.

Conditions of appointment, superannuation details, further particulars and application procedure available from the Association of Commonwealth Universities (Appis), 36 Gordon Square, London WC1H 0PF.

Applications close on November 26, 1973.

(1446)

WESTFIELD COLLEGE
(UNIVERSITY OF LONDON)

ELECTRON MICROSCOPE UNIT

requires a **TECHNICIAN GRADE 5** to take charge of the day-to-day running of the Electron Microscope suite and also to take an active part in training Postgraduates in Electron Micrography. The salary will be on the scale £2,007 to £2,382 plus London Allowance per annum. Applicants should hold an I.S.T. diploma in Electron Micrography and be able to use the AG1.801B microscope. Applicants without this qualification but willing to undergo training will also be considered but will be appointed on a lower grade.

Applications, giving full details and the names of two referees, should be sent to the Personnel Officer (N), Westfield College, Kidderpore Avenue, Hampstead, London NW3 7ST, by November 20, 1973. (1451)

**UNIVERSITY OF
WESTERN AUSTRALIA
PERTH**

MATHEMATICS

Applications for appointment as **SENIOR TUTOR** in the Department of Mathematics are invited from persons interested in any area of pure mathematics, applied mathematics, mathematical statistics or mathematical aspects of computation, and who expect to be available to assume duty before March 1974. Candidates should possess an Honours degree or the equivalent, but applications from students who expect to obtain such a qualification before taking up appointment will be considered. The salary range is: \$A7,270-\$A8,698 per annum. Benefits include superannuation similar to F.S.S.U., fares to Perth for appointee and dependent family, removal allowance, long service/study leave, and housing loan scheme. Further information is available from the Chairman of the Department, Professor J. J. Mahony, in the University.

Applications in duplicate, stating full personal particulars, qualifications and experience, should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia 6009, by 24 November 1973. Candidates should request three referees to write immediately to the Staffing Officer. (1447)

MALE GRADUATE (OR H.N.C.) BIOLOGIST required to join a team working in respiratory physiology and inhalation toxicology. Studies are being made into the effects on Primates and Rodents of exposure to cigarette smoke, air pollutants, and therapeutic aerosols. Salary range £1,400-£2,800 depending upon experience.—Application form from: John Halliday, Personnel Officer, Huntingdon Research Centre, Huntingdon PE18 6ES, quoting Reference 279. (1448)

SURREY EDUCATION COMMITTEE

EWELL COUNTY TECHNICAL COLLEGE
Reigate Road, Ewell

DEPARTMENT OF BIOLOGICAL SCIENCES

Required January 1974:

LECTURER I OR II IN PLANT PATHOLOGY to teach up to M.I.Biol. level (Honours degree equivalent).

Candidates should have a 1st degree in an appropriate Biological subject and preferably a higher degree in Plant Pathology. Industrial and/or teaching experience also an advantage.

The Department encourages research either independent of or under the guidance of the Research Director.

Salary: Lecturer I, £1,660 to £2,685 per annum (£2,847 per annum for good Honours graduate); Lecturer II, £2,515 to £3,243 per annum. £118 per annum London Allowance payable.

Generous relocation expenses and assistance with house purchase in approved cases.

Stamped, addressed foolscap envelope, please, for further particulars and application form from the Vice Principal; applications to be returned within 10 days. (1417)

UNIVERSITY OF LEICESTER

DEPARTMENT OF PHYSIOLOGY

LECTURER

Applications are invited for the post of **LECTURER** in the Department of Physiology (Head of Department, Professor R. Whitam, F.R.S.). An interest in teaching medical students is essential, and possession of a medical qualification desirable, but other suitably qualified applicants will be seriously considered. There are excellent research facilities.

Initial salary, dependent on qualifications and experience, within the scale £1,929 to £4,548 a year, with F.S.S.U. membership.

Further particulars from the Registrar, to whom applications should be sent by December 11. (1422)



**Imperial
Chemical
Industries
Limited**

**Industrial Hygiene
Research Laboratories**

Research Assistants

These Laboratories provide central advisory and experimental toxicological services to the Company. As well as evaluating the safety of industrial chemicals, food additives and pesticides, emphasis is placed upon improving and assessing methods for studying the biological effect of chemicals and upon understanding mechanisms of toxicity. Good experimental facilities are available and extensions are planned.

There are a number of interesting positions for men and women who have studied biology to a variety of academic levels (CSE to B.Sc.) and who would like a career in biological research work. Opportunities for further study can be given. Previous laboratory experience would be an advantage.

If you are interested in learning more about these vacancies, please contact:

Miss A. Waring
ICI Limited
Industrial Hygiene Research Labs
Alderley Park
Nr. Macclesfield, Cheshire SK10 4TJ
Tel: Alderley Edge 2711 ext 156

(1442)

**UNIVERSITY OF KHARTOUM
SUDAN**

Applications are invited for (a) **SENIOR LECTURESHIP** or (b) **LECTURESHIP IN VETERINARY SURGERY IN DEPARTMENT OF CLINICAL STUDIES** in Faculty of Veterinary Science. Applicants should possess a Ph.D. or equivalent in veterinary surgery and at least 2 years' teaching experience in veterinary surgery at university level. Appointee will be expected to teach veterinary surgery, including anaesthesia, to final and sub-final year students, do research in the Department, supervise postgraduate students for higher degrees, and participate in clinical and surgical work. Salary scales: Senior Lecturer £52,400 to £52,800 per annum; Lecturer £51,500 to £52,300 per annum (£1 sterling = £50.85). The British Government may supplement salary in range £1,300 to £1,600 per annum (sterling) for married appointee or £800 to £900 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. Family passages; various allowances; superannuation scheme; annual overseas leave.

Detailed applications (6 copies), including a curriculum vitae and naming 3 referees, should be sent not later than November 29, 1973, to the Personnel Secretary, University of Khartoum, P.O. Box 321, Khartoum, Sudan. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (1361)

JUNIOR TECHNICIAN

required by the Medical Research Council Unit and University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford. The work will be biochemical and pharmacological with clinical application. No previous experience is required, but the successful applicant will be expected to train for higher qualifications as a Laboratory Technician. Applicants should have at least 4 'O' levels, including English language and 2 science subjects, of which 1 should be mathematics. Salary will be within the scale £708 to £1,395, depending upon age and qualifications.

Applications should be sent to Professor D. G. Grahame-Smith. (1383)

THE R.S.P.B. REQUIRES A RESEARCH BIOLOGIST to investigate large-scale bird mortality and monitor seabird colonies. The work includes organising surveys of beached birds and of colonies of auks and terns. There will be opportunities for field research. Work is based at R.S.P.B. Headquarters, Sandy, and there is regular liaison with other organisations. Applicants should have university degree or equivalent and be competent ornithologists. Knowledge of seabirds, statistics or avian physiology as well as lecturing experience are an advantage. Salary in the range £1,450 by £60 to £1,810 per annum.—For further details and application form send s.a.e. to Mrs. Angela Legge, R.S.P.B., The Lodge, Sandy, Beds. SG19 2DL. (1386)

Institute of Aviation Medicine, Farnborough

Biophysicist

up to £4,575

To join an inter-disciplinary team studying the effects of high energy light on vision, and to be responsible for the optical and electronic aspects of physiological and behavioural studies on man and animals in this field.

Candidates should have a good honours degree in Biophysics or other relevant subject and must have had considerable research experience at a responsible level on lasers preferably with special reference to the biological effects of laser radiation.

Starting salary within the scale £3,472-£4,575 (Principal Scientific Officer grade) according to qualifications and experience with prospects of promotion. The appointment may be permanent and pensionable or, with the present employer's agreement, on secondment terms.

For full details and an application form (to be returned by 26 November 1973), write to Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, or telephone Basingstoke 29222, extension 500, or London 01-839 1992 (24-hour answering service). Please quote SJ8445/2.

(1443)

Ministry of Defence



South African Atomic Energy Board

PELINDABA

Plasma Physicists

A programme of research on laser-heated plasmas in a magnetic field is being undertaken with a view to future thermo-nuclear energy possibilities.

Applications are invited from persons with a Ph.D. degree in Physics who are interested in doing experimental or theoretical work in this field. Preference will be given to applicants with experience of plasma and laser physics. The commencing salary will be determined according to qualifications and experience.

Fringe benefits include: Medical Benefit Scheme, Assisted Housing loan scheme, housing subsidy scheme, Pension and Group Insurance Scheme, Annual Leave Bonus, ample leave privileges and free transport between Pretoria and the Board's site. A person appointed from overseas will receive financial assistance in regard to travelling expenses and the cost of transporting his furniture and effects including a motor car. He is required to make use of all assistance given by the South African Department of Immigration, the amount received from the said Department will be deducted from the financial assistance offered by the Board. He is also required to serve the Board for two years in consideration of the financial assistance received. A non-South African appointee must undertake to apply for South African Citizenship as soon as he qualifies therefor.

Written applications, giving full details of qualifications, experience, employer and salary, etc. should be addressed to:

South African Embassy, Office of the Scientific Counsellor, Chichester House, 278 High Holborn, LONDON WC1V 7HE (Telephone: 01-242 9641).

(1416)

UNIVERSITY OF NEW SOUTH WALES SCHOOL OF CHEMISTRY LECTURER

In the field of analytical chemistry for duties associated with undergraduate and postgraduate courses. High academic qualifications required, together with appropriate postgraduate experience in analytical chemistry and tertiary level teaching experience.

Salary: \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on 14 December 1973. (1424)

CHELSEA COLLEGE UNIVERSITY OF LONDON

TECHNICIAN (GRADE 3) required in the Analytical Laboratories of the Chemistry Department. Candidates should have a good basic university technical training, experience in the use of spectrophotometers, tools, etc., and be able to do simple glass blowing. Salary scale £1,825 to £2,095 per annum (including London Allowance).

Application forms from the Superintendent of Laboratories (N), Department of Chemistry, Chelsea College, Manresa Road, London SW3 6LX. (1428)

THE UNIVERSITY OF ADELAIDE

Applications are invited for the following appointments:

LECTURER IN BOTANY from beginning of 1974, to teach at both undergraduate and postgraduate levels in ecology, higher degree required. Field should be relevant to current environmental problems and might include plant ecology, general ecology (provided interests embrace plants) or related topics such as phytoplankton and marine productivity or physiology of plants under stress. (15.12.73.)

TEACHING FELLOW IN ORGANIC CHEMISTRY for 1974 from candidates with Ph.D. degrees; to be responsible for practical courses including course innovations and to undertake research with existing research groups, which enjoy modern facilities of high standard. (7.12.73.)

Salary scales: Lecturer \$A8,698 by 470(1) by 469(6) to 11,982; with superannuation on the F.S.S.U. basis; Teaching Fellow \$A7,270 by 286(3) by 285(2) to 8,698; a non-superannuated and non-tenured appointment.

Further particulars about these posts and the conditions of appointment and other information sought will be supplied on request to the Registrar of the University, or to the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications should be sent in duplicate and giving the information listed in the statement that will be supplied, to the Registrar, the University of Adelaide, North Terrace, Adelaide, South Australia 5001. (1427)

UNIVERSITY OF RHODESIA

FACULTY OF SCIENCE

LECTURESHP IN ANIMAL SCIENCE

Applications are invited for the post of Senior Lecturer or Lecturer in Animal Science in the Department of Agriculture. Candidates should have at least an honours degree in agricultural science together with relevant research experience and a knowledge of animal production. A special knowledge of either animal physiology or livestock improvement is essential.

Salary Scale (Approx. stg. equiv.): Lecturer Grade II: £2,711 by £133 to £3,110 by £160 to £4,230; Lecturer Grade I: £4,390 by £160 to £5,030; Senior Lecturer: £4,844 by £186 to £6,332.

Family passages and allowance for transport of effects on appointment. Installation loan of up to half of one year's salary if required. Unfurnished University accommodation guaranteed for a period of at least three years for persons recruited from outside Rhodesia. Sabbatical and triennial visits with travel allowance. Superannuation and medical aid schemes.

Applications (6 copies), quoting Ref. No. UK/29/73 and stating where advertisement seen, and giving full personal particulars (including full names, place and date of birth etc.), qualifications, experience and publications, and naming three referees should be submitted by 17 November 1973, to the Assistant Registrar (Science), University of Rhodesia, P.O. Box MP 167, Mount Pleasant, Salisbury, Rhodesia, from whom further particulars can be obtained. Additional copy to the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF, from whom further

ZOOLOGICAL SOCIETY OF LONDON

ASSISTANT EDUCATION OFFICER

A graduate in Zoology is required to lecture and demonstrate at London Zoo and, during the summer, Whipsnade Zoo to pupils of varying abilities ranging in age between 8 and 18 plus years.

Previous teaching experience would be an advantage but is not essential. An interest in photography and the production of tape/slide materials would be an added recommendation.

Other duties involved are concerned with the meetings and magazine of the Young Zoologists' Club, in information work, and in assisting with administrative work.

The salary is Burnham Scale 2 plus London weighting. Annual leave is 18 working days.

The successful candidate should be prepared to take up the post in the new year. Detailed applications in writing should be sent to:

**The Establishment Officer,
Zoological Society of London,
Regent's Park, London NW1 4RY.**

(1454)

NEWCASTLE UPON TYNE POLYTECHNIC

Ellison Building, Ellison Place, Newcastle upon Tyne NE1 8ST

Required as soon as possible

Department of Materials Science

RESEARCH ASSISTANTS

are required for research projects financed by the Science Research Council and the Ministry of Health. One post is for a study of the products of burning plastics and the other is for applications of plastics reinforced with carbon and other fibres.

Suitable graduates may be permitted to register for a higher degree.

Salary scale: Research Assistant £1,200 to £1,500.

Further information may be obtained from Dr. T. R. Manley at the above address.

(1406)

MONASH UNIVERSITY MELBOURNE, AUSTRALIA

DEPARTMENT OF EARTH SCIENCES

SENIOR LECTURER/LECTURER

Applications are invited for the position of Lecturer/Senior Lecturer in the Department of Earth Sciences in the Faculty of Science. Preference will be given to applicants with interests in hard-rock geology (including igneous, metamorphic and sulphide petrology, experimental petrology and structural geology). The department is developing well equipped experimental, analytical and electron microscopy laboratories and it is intended that the successful applicant should have interests compatible with these lines of research.

Salary scale: Senior Lecturer: \$A12,268 to \$A14,308 per annum. Lecturer: \$A8,698 to \$A11,982 per annum, with superannuation based on an endowment assurance scheme, the employee and employer contributing 5% and 10% respectively.

Benefits: Travelling expenses for appointee and family; removal allowance; repatriation after three years' appointment if desired; temporary housing for an initial period; availability of loans for home purchase; study leave entitlement accumulates at the rate of one month's leave for each six months' service up to six years, with provision for financial assistance.

Further general information and details of application procedures are available from the Academic Registrar, Monash University, Wellington Road, Clayton, Victoria 3168, Australia, or the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF. Enquiries about the department should be sent to the Chairman, Professor B. E. Hobbs, in the University.

Closing Date: December 1, 1973.

The University reserves the right to make no appointment or to appoint by invitation. (1433)

ROYAL POSTGRADUATE MEDICAL SCHOOL

GRADUATE TECHNICAL OFFICER (Microbiology) required to work in the Routine Diagnostic Bacteriology Laboratory. Applicants should have had previous experience in a clinical laboratory. Salary according to qualifications and experience but not less than £1,800 per annum.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, W12 0HS, quoting reference 5/125/N. (1434)

Have you ever considered becoming a MEDICAL REPRESENTATIVE?

CAT is the consultancy specialising exclusively in the medical and pharmaceutical industries. We are now looking for men to fill key positions in both the hospital and G.P. fields in several parts of the country.

If you are 22-30 and looking for a new and worthwhile development in your career which can offer you a high immediate salary ring 01-794 6298 or write to:

Career Appointments and Training, 36 Grosvenor Street, Mayfair, London W1X 9FG. (1421)

UNIVERSITY OF NEW SOUTH WALES

WOLLONGONG UNIVERSITY COLLEGE
to become the
UNIVERSITY OF WOLLONGONG
on January 1 1975

PROFESSOR OF COMPUTING SCIENCE

Applications are invited for appointment to a second chair in the Department of Mathematics. Applicants should have particular interests in design and implementation of computer software. The professor will supervise and participate in teaching and examining undergraduate and postgraduate students in the Department and engage in and promote research and advanced study in the field of his chair. In addition he will develop new options within the Department of Mathematics for science and engineering students at both undergraduate and postgraduate levels.

Salary: \$A19,102 per annum. Subject to the consent of the University Council, professors may undertake a limited amount of higher consultative work. The University reserves the right to fill any chair by invitation.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on November 23, 1973. (1437)

UNIVERSITY OF HONG KONG LECTURES/ASSISTANT LECTURES/ASSISTANT ENGINEERING

Applications are invited for posts of Lecturer/Assistant Lecturer in Mechanical Engineering. Applicants should have some years of experience in industry. Preference will be given to persons with expertise in any of the following fields:

- Mechanics of machines and vibration.
- Strength of materials and mechanical properties.
- Environmental engineering.
 - Air conditioning and solar energy applications.
 - Desalination technology.

All applicants will be expected to take part in the teaching of part I subjects and to participate in a postgraduate teaching programme planned to start in October 1974. A graduate in chemical engineering could be an appropriate candidate to develop studies in desalination, besides teaching fluid mechanics and heat transfer.

Annual salaries (superannuable) are Lecturer: HK\$40,800 by 2,760 to 46,320 BAR 49,080 by 2,760 to 68,400; Assistant Lecturer: HK\$29,760 by 2,760 to 38,040. At the time of issue the rate of exchange is £1=HK\$12.00 approximately.

Starting salary will depend on qualifications and experience. Salaries for female appointees below HK\$62,880 are slightly lower than given above; equalization of male and female salary scales will be achieved by April 1, 1975.

Further particulars and application forms may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF, or the Secretary to the Council, University of Hong Kong.

Closing date for applications is December 5, 1973. (1436)

QUEENSLAND INSTITUTE OF TECHNOLOGY BRISBANE, AUSTRALIA SCHOOL OF APPLIED SCIENCE

QUOTE: V. 152.73

Within the Queensland Institute of Technology the School of Applied Science offers degree courses in Applied Chemistry, Biology, Computing Science, Mathematics, Medical Technology and Physics. In addition, postgraduate diplomas and master's degree courses in specific vocational areas are being planned for implementation in the near future. A number of undergraduate diploma courses are also organised within the School.

Applications are invited for the following academic appointments:

Department of Biology and Environmental Science
**SENIOR LECTURER IN FRESH WATER
PLANT PRODUCTIVITY**

Department of Chemistry
SENIOR TUTOR IN ORGANIC CHEMISTRY
Department of Mathematics and Computer Science
LECTURER IN FINANCIAL MATHEMATICS

SENIOR TUTORS (4 POSITIONS)

Department of Paramedical Studies

LECTURER IN OPTOMETRY

Department of Physics

SENIOR LECTURER/LECTURER

Salary Ranges:

Salary ranges for lecturing staff are normal Australian University rates.

Senior Lecturer \$12,268 to \$14,308 per annum.

Lecturer I \$8,698 to \$11,982.

Lecturer II \$7,165 to \$9,674.

Senior Tutor \$6,969 to \$7,855.

Further particulars and details of positions may be obtained from the Registrar, Queensland Institute of Technology, P.O. Box 246, North Quay, Brisbane, 4000.

Applications containing full personal particulars, details of qualifications and experience, and the names and addresses of two referees should be forwarded to the Registrar, at the above address. Closing date for receipt of applications is December 3, 1973. (1420)

NEW ZEALAND UNIVERSITY OF CANTERBURY Christchurch SENIOR LECTURER OR LECTURER IN ZOOLOGY (ANIMAL PHYSIOLOGY)

Applications are invited for the above-mentioned position. Experience and research interest in respiration, excitable tissues and/or sensory physiology are desirable.

The salary for Lecturers is on a scale from \$NZ6,575 to \$8,343 per annum, and for Senior Lecturers \$NZ8,489 to \$9,963 (bar) \$10,259 to \$10,846 per annum.

Particulars including information on travel and removal allowances, study leave, housing and superannuation may be obtained from the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close on November 30, 1973. (1435)

THE OPEN UNIVERSITY

Science Faculty

Technician Grade 4 in Chemistry

Applications are invited for the above post to be taken up as soon as possible.

Duties include the preparation of home experiments, summer school experiments, T.V. demonstrations and in particular assisting with research within the discipline.

Salary within the scale: £1,848-£2,163 per annum.

Further particulars may be obtained from The Acting Personnel Manager (C2), The Open University, P.O. Box 75, Walton Hall, Milton Keynes MK7 6AL.

Applications should be returned as soon as possible.

(1450)

UNIVERSITY OF
NEW SOUTH WALES
WOLLONGONG UNIVERSITY COLLEGE
to become the
UNIVERSITY OF WOLLONGONG
on January 1, 1975

PROFESSOR OF BIOLOGY

Applications are invited for appointment to the above-mentioned chair in the Division of Biological and Chemical Science. Applicants should have interests in all branches of biology but the University is particularly interested in attracting candidates with a background in ecology or physiology. The appointee will contribute to the development of a complete biological programme and will supervise and participate in teaching and examining undergraduate and postgraduate students and engage in and promote research and advanced study in the field of his chair.

Salary: \$A19,102 per annum. Subject to the consent of the University Council, professors may undertake a limited amount of higher consultative work. The University reserves the right to fill any chair by invitation.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on November 23, 1973.

(1432)

TECHNICIANS (2) REQUIRED IN BACTERIOLOGY DEPARTMENT for research with group investigating immune defences to bacterial infections. Salary according to age, experience and qualifications within scale £1,440/£2,292 per annum plus £126 per annum L.W.—Apply, The Secretary, St. Mary's Hospital Medical School, Paddington, W2 1PG.

(1455)

Scottish National Blood Transfusion Association NON-MEDICAL SCIENCE GRADUATE (PRINCIPAL GRADE) IN THE REGIONAL TRANSFUSION CENTRE, LAW HOSPITAL

Applications are invited for a scientist to head a small team of graduates in a progressive regional transfusion centre. The post is suitable for a graduate in biochemistry or a biological discipline; previous experience in blood transfusion is not essential. Possession of a higher degree is desirable.

In addition to research there are opportunities for teaching at undergraduate and postgraduate level. The laboratories are modern and in pleasant surroundings.

The post is superannuable (N.H.S. Superannuation Scheme).

Further details may be obtained from the under-mentioned to whom applications, with names and addresses of two referees, should be sent by not later than November 23, 1973.

Neil A. Milne, WS, Secretary,
Scottish National Blood Transfusion
Association,
5 St. Colme Street,
Edinburgh EH3 6AE.

(1456)

UNIVERSITY OF RHODESIA

FACULTY OF ARTS

Applications are invited for:

SENIOR LECTURESHIPS/LECTURESHIPS IN GEOGRAPHY (Two Vacancies): Applicants should indicate the full range of their interests and abilities as well as their special field. For one post, preference may be given to applicants with qualifications in biogeography (preferably with wide interests in vegetation studies) and, for the second, in the general field of human geography, but applications from any well-qualified persons are invited. Ability to teach a course in the regional geography of an area other than N.W. Europe and Africa may be a secondary recommendation.

Salary scales (approx. stg. equiv.): Senior Lecturer: £4,844 by £186 to £6,332; Lecturer Grade I: £4,391 by £160 to £5,031; Lecturer Grade II: £2,711 by £133 to £3,110 by £160 to £4,230.

Family passages and allowance for transport of effects on appointment. Assistance with accommodation for up to three years for persons recruited from outside Rhodesia. Sabbatical and triennial visits with travel allowance. Superannuation and medical aid scheme.

Applications: (6 copies) giving full personal particulars (including full names, place and date of birth, etc.), qualifications, experience and publications and naming three referees, should be submitted by November 30, 1973, to the Registrar, University of Rhodesia, P.O. Box MP 167, Mount Pleasant, Salisbury, Rhodesia, from whom further particulars may be obtained. Additional copy to the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF, from whom further particulars may also be obtained.

(1431)

BEDFORD COLLEGE

(UNIVERSITY OF LONDON)

Department of Physics

Applications are invited from suitably qualified graduates in mathematics, physics, or chemistry for the post of

RESEARCH ASSISTANT/PROGRAMMER

under a 3-year grant from the Science Research Council. The appointee will be working under the direction of Dr. M. R. Hoare on the statistical mechanics and microcrystallography of small atomic and molecular clusters. Excellent computing facilities are available. Appointment for 1 year in the first instance from 1 January, 1974, or an earlier agreed date.

Salary within the range £1,572 by increments to £1,923 per annum.

Application forms and further particulars may be obtained from the Assistant Secretary (Personnel) (N), Bedford College, Regent's Park, London NW1 4NS. Telephone (01) 486 4400, Ext. 313.

(1429)

FELLOWSHIPS AND STUDENTSHIPS

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF CHEMISTRY

Applications are invited for a Postdoctoral Fellowship in Inorganic Chemistry. Interests in organometallic chemistry, nuclear magnetic resonance spectroscopy, high temperature chemistry, high resolution spectroscopy, or mass spectrometry.

Apply, giving a brief curriculum vitae and the names of two referees, to Professor I. R. Beattie, Department of Chemistry, The University, Southampton SO9 5NH, quoting Ref. Na. (1373)

UNIVERSITY OF SOUTHAMPTON

DEPARTMENT OF ELECTRICAL ENGINEERING

RESEARCH FELLOWSHIP

A challenging research post is available for a period of up to three years to work on magnetic-field problems in turbogenerators with superconducting rotors. Suitable candidates will have some industrial experience or a higher degree, a knowledge of electrical machines and electromagnetism, and, above all, enthusiasm for the subject. The initial salary will be up to £2,553, plus annual increments of £165. F.S.S.U. membership is available.

Applications, giving details of age, qualifications and experience, together with the names of two referees, should be sent to the Deputy Secretary's Section (Ext. 2400), The University, Southampton SO9 5NH, not later than November 25, 1973. Please quote Reference Na286/R.

(1374)

ASSISTANTS AND FELLOWSHIPS

available for graduate study in materials science and engineering leading to M.S. and Ph.D. Research areas include mechanical properties, crystal growth, surfaces, corrosion, electronic properties, biomaterials, fuel cells and batteries, phase transformations and materials synthesis and processing.

For information write: Chairman, Department of Materials Science and Engineering, Stanford University, Stanford, California 94305.

(1380)

EDINBURGH CORPORATION

NAPIER COLLEGE OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF MATHEMATICS AND COMPUTING

Applications are invited for a FELLOW-SHIP for a project within the National Development Programme in Computer Assisted Learning. Applicants should be computer scientists with postgraduate experience to Ph.D. level. Experience of algebraic manipulators would be an advantage.

The appointment will be for 16 months in the first instance and the salary will be £2,100 per annum.

Further particulars and application forms from the Principal, Napier College of Science and Technology, Colinton Road, Edinburgh EH10 5DT, to whom they should be returned by November 23, 1973, quoting Reference Number N/231. (1369)

UNIVERSITY OF MELBOURNE

JUNIOR RESEARCH FELLOW IN MARINE BACTERIOLOGY

in the SCHOOL OF MICROBIOLOGY

Applications are invited for this position.

QUALIFICATIONS: The successful applicant should hold a Ph.D., have had research experience in marine or aquatic bacteriology, and be capable of independent research.

DUTIES: The Fisheries and Wildlife Department of the State of Victoria is co-ordinating a Pollution Survey of Port Phillip Bay. The Junior Research Fellow will study the bacterial flora of different representative environments in the Bay, to evaluate the effects of current practices of water management. These results will be co-ordinated by the Fisheries Department with studies of other parameters and used to construct a mathematical model of the Bay. The bacteriological research will be done in the School of Microbiology, and technical assistance will be provided; facilities for field work will be provided through the Fisheries and Wildlife Department.

SALARY: \$A7,556 in the first instance, with annual increments to \$A8,128. Limited assistance is available for travel to Australia for an overseas applicant.

The successful applicant would be required to begin duties in January 1974 and the grant is available for 3 years from that date. Further information can be obtained from Dr. N. F. Millis, School of Microbiology, University of Melbourne, Parkville 3052, Victoria, Australia.

Details of application procedure are available from the Registrar, University of Melbourne, Parkville 3052, Victoria, Australia. Applications, referring to Position No. B/2/73 and including the names of at least two referees, should be addressed to the Registrar and close on December 5, 1973. (1426)

THE UNIVERSITY OF SHEFFIELD

DEPARTMENT OF MEDICAL MICROBIOLOGY

Applications are invited for an M.R.C. POST-DOCTORAL FELLOWSHIP, tenable as soon as possible. The successful candidate would work on the departmental programme of research on the pathogenesis of gonococcal infections. The salary will be in the range for University Lecturers according to qualifications and experience. Further particulars from the Registrar and Secretary to whom applications should be sent by November 23, 1973. Quote Ref. R/87/G. (1438)

ROYAL FREE HOSPITAL

SCHOOL OF MEDICINE

(UNIVERSITY OF LONDON)

JUNIOR RESEARCH FELLOWSHIP

Applications are invited from graduates with an Honours degree in physiology, with some biochemistry, to work in the Department of Physiology in the transfer of substances, particularly folates, across the placenta. The successful applicant will be expected to register for a higher degree. Value of the Fellowship is £1,344 per annum and the appointment will be limited to three calendar years.

Applications and requests for further information should be addressed to Professor C. B. B. Downman, Royal Free Hospital School of Medicine, 8 Hunter Street, London WC1N 1BP. (1403)

POLYTECHNIC OF THE SOUTH BANK

DEPARTMENT OF MATHEMATICS

RESEARCH FELLOW

(Ref. X.23)

Candidates may offer any suitable field of mathematics, computer science, statistics or operational research. They should normally have completed a three-year course of postgraduate training and have shown an aptitude for original and independent research. Fellowships are usually held for a period of two years. Salary £1,984 to £2,239 per annum.

Further particulars and application forms from the Clerk to the Council (Room 538), Polytechnic of the South Bank, Borough Road, London SE1 0AA. Tel. 01-928 8989. (1377)

THE LEVERHULME TRUST

Research Awards 1974

The Leverhulme Trustees, through their Research Awards Advisory Committee, offer:

(i) FELLOWSHIPS AND GRANTS—

To assist senior persons pursuing investigations, particularly those who are prevented by routine duties or any other cause from undertaking or completing a research programme. These awards are not available for persons reading for higher degrees or equivalent awards. No subject of enquiry is excluded from consideration.

The awards are limited to persons educated in the United Kingdom or in any other part of the Commonwealth who are normally resident in the United Kingdom. The duration of the awards does not extend over more than two years or less than three months, and the amount of the award depends on the nature of the work and the circumstances of the case.

The closing date for applications (Form F/2C) is December 1, 1973. The period of award may start from June 1, 1974.

(ii) EMERITUS FELLOWSHIPS—

A limited number of awards to assist persons who have recently retired or who are about to retire from academic positions in universities or institutions of similar status in the United Kingdom and who have an established record of research. They are designed to help in the completion and preparation for publication of the results of such research.

The award attached to the fellowship is to meet incidental costs such as typing, secretarial or research assistance, books, photostats, preparation of plates or blocks, apparatus or equipment, travel and subsistence away from home for essential visits to libraries and other sources of original material. It is not normally intended to provide a personal allowance or a pension supplementation. The fellowships are tenable for one or two years and are not thereafter renewable. The amount of the award depends on the nature and cost of the assistance sought but does not exceed a rate of £2,000 a year.

The closing date for applications (Form F/6C) is December 1, 1973. The period of award will normally date from June 1, 1974.

(iii) FACULTY FELLOWSHIPS IN EUROPEAN STUDIES—

A limited number of awards to strengthen the teaching of European Studies in the universities of this country. These awards are intended to assist established members of the staffs of universities in the United Kingdom to undertake advanced study or research in a European country or countries excluding the British Isles in their particular fields of interest. The fellowships are designed to enable scholars in this country directly to consult their academic colleagues in Europe and to have access to sources of original materials.

The fellow must spend at least six months in Europe normally in not more than two separate periods.

The award attached to the fellowship may be expected to cover the direct costs involved in the fellow's study programme such as subsistence while abroad, travel to and from the European country or countries in which the fellow wishes to study, internal travel within the country or countries and other incidental expenses. The award will not normally provide for salaries or personal allowances. It will vary as to amount to meet the circumstances of each case, but will not normally exceed the rate of £250 a month with a maximum total value of £2,000.

The closing date for applications (Form FF/10C) is December 31, 1973. The period of award may start from June 1, 1974.

(iv) OVERSEAS STUDENTSHIPS—

Up to six studentships for a period of advanced study or research in any subject at an institution of university or university college status in any part of the world other than the United Kingdom, Europe or North America.

At the time of application candidates should be graduates of a United Kingdom university, holders of C.N.A.A. degrees or able to show evidence of equivalent education. They should also have been educated at a school or schools in the United Kingdom or in any other part of the Commonwealth. They must be normally resident in the United Kingdom and under the age of 30 on October 1 in the year of the award.

The value of the studentships is £1,000 per annum. In addition, an amount of £200 will be provided towards outfit and return passages; additional assistance will be available where the cost of the student's return passage exceeds £180 or to meet abnormal requirements connected with the course of study. A further allowance of £25 per month may be paid, at the discretion of the Committee, to a married student when accompanied by his wife.

The awards are tenable for one year or two years if circumstances warrant it. The awards may not normally be held in conjunction with other major awards. Students will be asked on termination of an award to make a short report to the Committee on their experience during the period of study.

Candidates must be available for interview in London late in March; travelling expenses within the United Kingdom will be refunded. Successful candidates will be required to undergo a medical examination before confirmation of their awards.

The closing date for applications (Form O/2C) is January 15, 1974. The period of award will normally date from October 1, 1974.

(v) EUROPEAN STUDENTSHIPS—

Up to eight studentships of £1,200 for one year for advanced study or research in a centre of learning in any European country other than the United Kingdom or Ireland. A further allowance of £25 per month may be paid, at the discretion of the Committee, to a married student when accompanied by his wife.

At the time of application candidates should be graduates of a United Kingdom university, holders of C.N.A.A. degrees or able to show evidence of equivalent education. They should also have been educated at a school or schools in the United Kingdom or in any other part of the Commonwealth. They must be normally resident in the United Kingdom and under the age of 30 on October 1 in the year of the award.

The studentships are tenable only at or in connection with a university, college or similar institution. They are not intended for students of modern languages; otherwise no subject of study will be excluded but preference will be given to candidates who intend to study in subjects normally grouped in the Arts and Social Studies Faculties of universities.

The period of award normally begins on October 1 and students will be required on termination of the award to make a short report to the Committee on their experience during the year of study. The awards may not normally be held in conjunction with another major award.

Candidates must be available for interview in London in the second half of April; travelling expenses within the United Kingdom will be refunded.

The closing date for applications (Form E/2C) is January 15, 1974. The period of award will normally date from October 1, 1974.

The results of applications for all the above awards will be communicated to the candidates in April, 1974. Application forms and further information from The Secretary, Research Awards Advisory Committee, The Leverhulme Trust, 21/23 New Fetter Lane, London EC4A 1NR. Telephone: 01-248 1910.

(1379)

UNIVERSITY OF NEW ENGLAND
ARMIDALE, NEW SOUTH WALES

TEACHING FELLOW IN GEOPHYSICS

Applications are invited from graduates with a degree in Geophysics, Physics, Geology and Mathematics, or Electronic Engineering, for this appointment commencing April 29, 1974. Duties will involve the development and supervision of student practical work, together with research work in the development and field testing of various geophysical instruments.

Salary range: \$A5,740 to \$A7,015 (base plus 5 annual increments).

Assistance is given with travel and removal.

Further information can be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF.

Applications close on 28 November 1973.

(1425)

GRANTS & SCHOLARSHIPS

£600 POST-GRADUATE GRANTS

MSc Dairy Science at Reading University

The Dairy Industry offers a limited number of special grants worth £600, plus all fees, for the one-year MSc course in Dairy Science at Reading University.

This post-graduate course is available to holders of first degrees or equivalent qualification in pure or applied science (including agriculture).

The awards are designed for those students who show outstanding potential for responsible scientific, technical and managerial positions in the processing and manufacturing sides of the Dairy Industry.

The MSc qualification could also lead to lectureships in dairy science and technology.

Applicants must be resident in the United Kingdom, and intent upon taking up employment in the United Kingdom Dairy Industry on completion of the course. All applications for the 1974 award must reach us by 31 January 1974.

For full details, please write to, or telephone:

Mrs Jacqueline Gray, Department 66,
The Dairy Industry Training
& Education Committee,
The Joint Committee, Giggs Hill Green,
Thames Ditton, Surrey KT7 0EL
Tel: 01-398 4101, Ext. 436.

(1368)

FRENCH GOVERNMENT SCHOLARSHIPS FOR further study and postgraduate research in France in Pure and Applied Science, Technology, Medicine, Social Sciences, Economics, Geography and Agriculture are offered for the academic year 1974-1975. Candidates, who must be United Kingdom citizens, should be university graduates or have equivalent qualifications. Closing date: December 31, 1973. —Details from Scientific Department, French Embassy, 41 Parkside, Knightsbridge, London SW1X 7JP. Citizens of the Commonwealth and of other countries should apply to French Embassies in their respective countries. (1309)

UNIVERSITY OF STRATHCLYDE

Department of Biochemistry

M.R.C. SCHOLARSHIP

A scholarship is available for up to three years, in the Department of Biochemistry, for work on ornithine decarboxylase in Reproductive Tissues. The scholar, who should possess a First or Upper Second Class Honours Degree in Biochemistry or cognate discipline, would be registrable for a Higher Degree, and would work closely in conjunction with the M.R.C. research group in Biochemistry of Reproduction, established within the Department.

Applications to Professor P. J. Heald, Department of Biochemistry, Royal College Building, University of Strathclyde, 204 George Street, Glasgow G1 1XW, from whom further information can be obtained. (1453)

POSTDOCTORAL FELLOWSHIP
for TEXTURE RESEARCH

Applications are invited for a post of Research Fellow to work on texture research. The research would involve the study of applications of crystallite orientation distribution function analysis in the study of texture, metal deformation and formability. The appointment is for a period of three years with a salary depending on age in the range £1,929 (age 24) to £2,388 (age 27) with provision for annual increments. Previous experience in texture research would be an advantage but is not necessary. Applications, including a brief curriculum vitae, research experience and the names and addresses of two referees, should be sent to Dr. G. J. Davies, Department of Metallurgy and Materials Science, University of Cambridge, Pembroke Street, Cambridge CB2 3QZ. (1440)

UNIVERSITY OF STRATHCLYDE

Department of Pharmaceutical Technology

RESEARCH STUDENTSHIP

An opportunity arises for a young graduate with suitable qualifications to undertake research for three years leading to Ph.D. The field of study may be chosen from one of the principal research activities of the department, viz. cell studies, bioavailability of drugs, microbiological pharmacy, effects of drugs on enzymes.

Financial support on S.R.C. (research studentship) scale is available.

Apply in the first instance to Professor W. Anderson, Department of Pharmaceutical Technology, Royal College Building, University of Strathclyde, 204 George Street, Glasgow G1 1XW. (1411)

EUROPEAN MOLECULAR BIOLOGY ORGANIZATION

ANNOUNCEMENT

EMBO WORKSHOP
ON PROTOPLASTS OF PLANTS AND FUNGI AS
GENETIC SYSTEMS

The WORKSHOP will be held at the Department of Botany, University of Nottingham, U.K., from July 29 to August 2, 1974. The programme will include some practical work and demonstrations, and discussions on: the development of plant and fungal protoplasts in culture; fusion and heterokaryon formation using plant and fungal protoplasts and aspects of somatic hybridisation; uptake of viruses by plant and fungal protoplasts and aspects of virus infection and transduction; and the general use of plant and fungal protoplasts as genetic systems.

Participation is limited to 40-50 persons. Applications should contain name, age, address, place of work and position held, reasons for wanting to attend the Workshop, and the name of one referee. Applications should be sent by January 1, 1974, to Professor E. C. Cocking, Department of Botany, University of Nottingham, University Park, Nottingham NG7 2RD, U.K. Notification of acceptance will be given early in 1974. All accommodation expenses at Nottingham will be covered by EMBO and a limited amount of travel support will be available for younger workers. (1385)

INSTITUTE OF CONNECTED EDUCATION

offer prizes for research in pure general science. That is, research in interdisciplinary sciences, or if and how all sciences are interconnected. Main object of the Institute is to create and sponsor the acceptance of a course of this nature in schools, colleges and institutes.

For further information please apply in writing to: The Secretary, Institute of Connected Education, 28a Cadogan Place, London SW1X 9RX. (1388)

QUEEN'S UNIVERSITY OF
BELFASTDEPARTMENTS OF
BIOCHEMISTRY AND MEDICINE
POSTDOCTORAL RESEARCH
FELLOWSHIP

Applications are invited for an M.R.C. sponsored Postdoctoral Research Fellowship to collaborate on the chemical and physiological characterisation of polypeptides from gut which have immunoreactive properties of a glucagon. Radioimmunoassays and affinity chromatography on solid-phase antibodies are routinely used in this work.

Applicants should have experience in protein chemistry.

The appointment is for three years, with a salary scale of £1,929—£2,058—£2,223 plus F.S.S.U.

Further particulars, if desired, may be obtained from Personnel Department, The Queen's University of Belfast, Belfast BT7 1NN, where applications should be received by November 19, 1973. (1413)

LECTURES AND COURSES

UNIVERSITY OF BIRMINGHAM
M.Sc. COURSES AND RESEARCH
FACILITIES

Applications are invited for admission to the following one-year M.Sc. courses which may be offered commencing in September/October 1974:

Analytical Chemistry; Applied Genetics; Brewing Science; Clinical Biochemistry; Clinical Psychology (two-year course); Conservation and Utilization of Plant Genetics Resources; General Virology; Immunology; Meteorology and Climatology; Neurocommunications; Radiobiology.

Details of these courses and of the facilities which are available for those students wishing to undertake research leading to the degrees of Ph.D. and M.Sc., together with forms of application for admission, may be obtained from the Assistant Registrar (S), University of Birmingham, P.O. Box 363, Birmingham B15 2TT, quoting PG.7. (1396)

UNIVERSITY OF LONDON: A LECTURE entitled "Crystal Chemistry of Mercury" will be delivered by Professor D. Grdenić (Zagreb) at 6 p.m. on November 13 at Birkbeck College, Department of Chemistry, Malet Street, W.C.1. Admission free, without ticket.—Academic Registrar. (1355)

UNIVERSITY OF LONDON: A LECTURE entitled "Surface Forces, Surface Energy and Adhesion" will be delivered by Dr. David Tabor (Cambridge) at 5 p.m. on November 8 at Birkbeck College (Large Chemistry Lecture Theatre), Malet Street, W.C.1. Admission free, without ticket.—Academic Registrar. (1356)

UNIVERSITY OF LONDON: A LECTURE entitled "Kepler: A Nightmare to Philosophers of Science" will be delivered by Professor Kurt Hübner (Kiel) at 5 p.m. on November 9 at the London School of Economics and Political Science, Houghton Street, Aldwych, W.C.2. Admission free, without ticket.—Academic Registrar. (1357)

LASERS IN
COMBUSTION
RESEARCH

A post-experience course of nine lectures arranged by Professor F. J. Weinberg will be given in the Department of Chemical Engineering and Chemical Technology, Imperial College, London S.W.7, from December 11-14, 1973.

Details from the Registrar. (1366)

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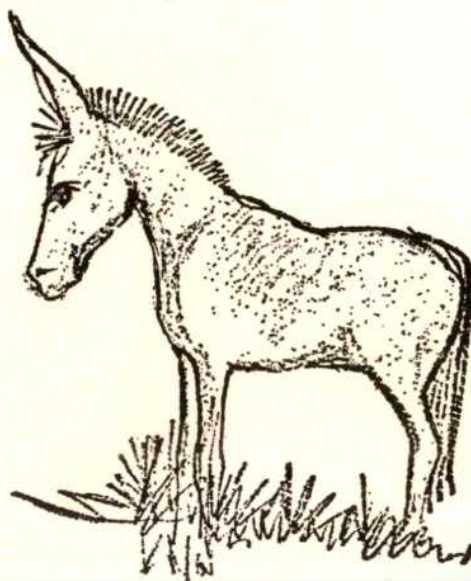
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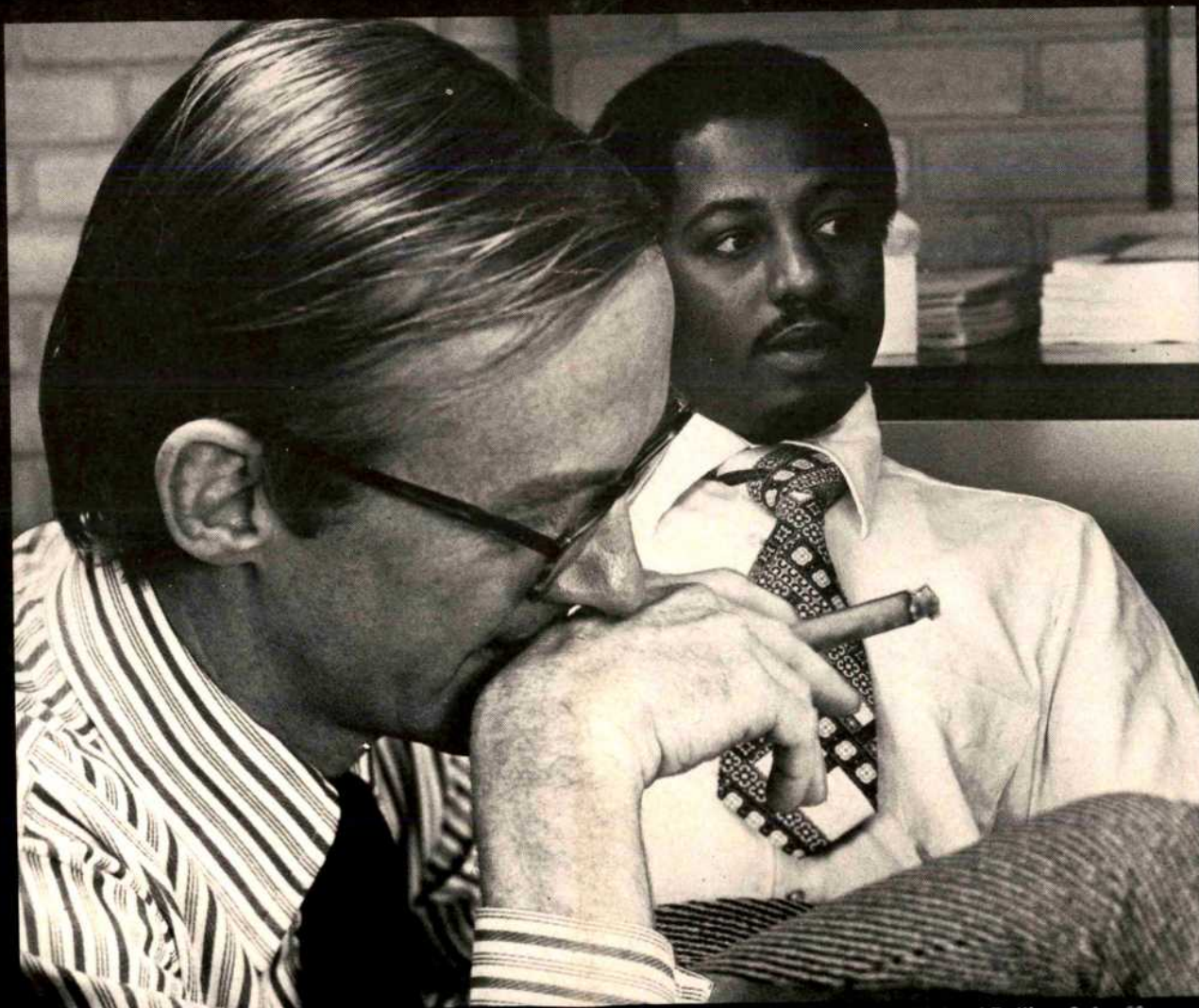
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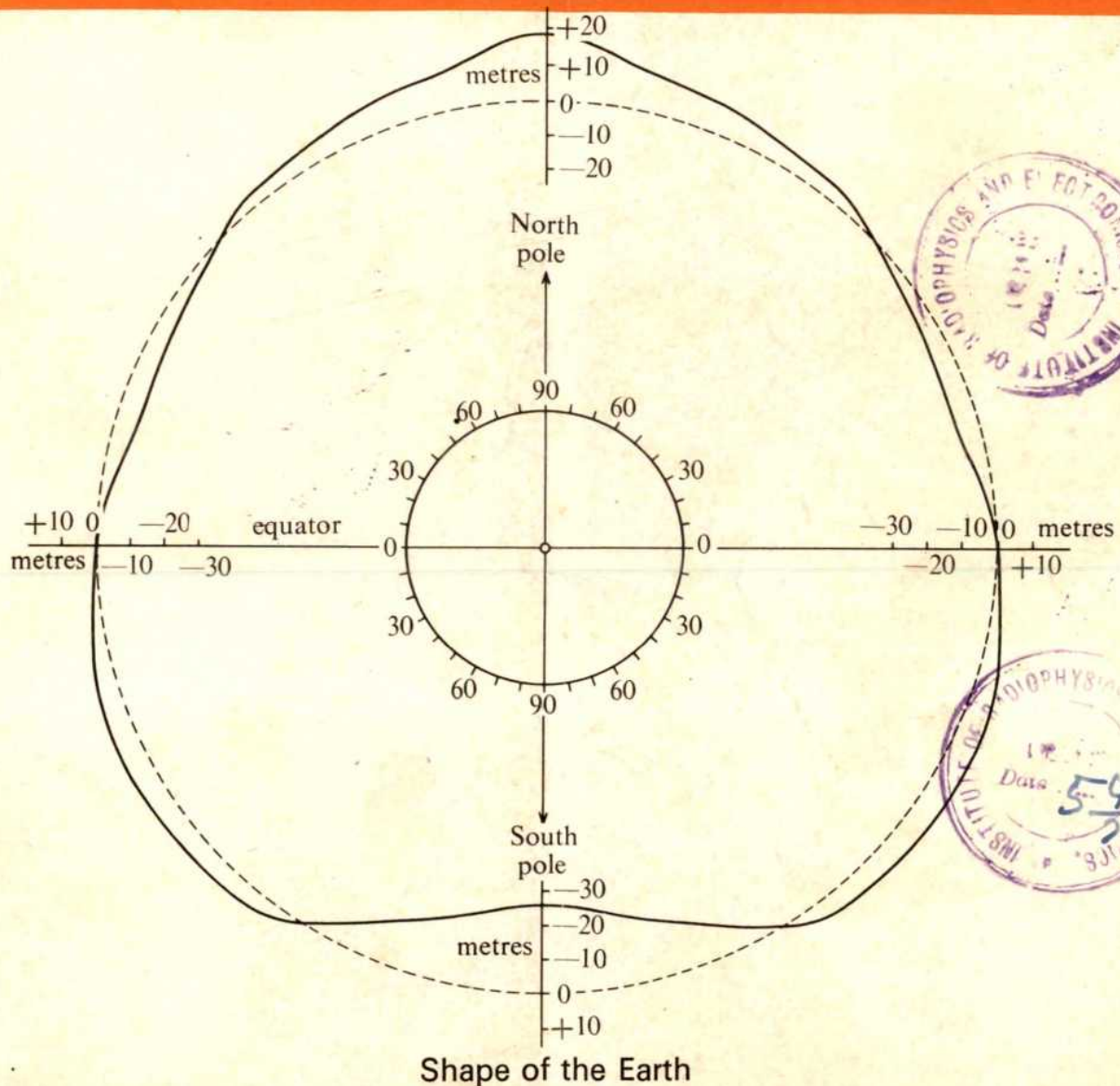


NATURE

Vol 246 No 5428

November 9 1973

FRIDAY



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Concorde eclipse observations
Ascitic tumours and lymphocyte trapping
Calcium in sickle cell disease



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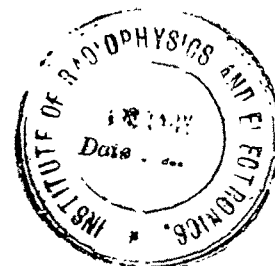
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	Page
The Ethiopian Calamity	53
The Problem of Compensation for Antenatal Injuries	54

NEWS

Canadian Societies seek More Involvement/Medical Jurisprudence	56
--	----

NEWS AND VIEWS

Hot Spots on X-ray Sources/Lymphocyte Trapping/Epidemiology/Ribosomal RNA/Wildlife/Herbaria/Cell Membrane/Insect Metamorphosis/Protein Synthesis / Peat / Plate Tectonics / Liquid Helium / Crystal Growth/Phytopathology	58
---	----

ARTICLES

Irreversibility as a Symmetry-breaking Process—PRIGOGINE (Brussels and Austin, Texas)	67
Sun—Concorde observations of eclipse—BECKMAN (Queen Mary College, London), BEGOT (Institut d'Astrophysique, Paris), CHARVIN (Institut National Astronomie et Géophysique, Meudon), HALL (Kitt Peak National Observatory), LENA, SOUFFLOT (Observatoire de Meudon), LIEBENBERG (Los Alamos) and WRAIGHT (Aberdeen)	72
Geomorphology—Dating of cave openings at sites of South African hominids—PARTRIDGE (Braamfontein, South Africa)	75
South African hominids—Implications of the new age estimates of the South African sites—TOBIAS (Witwatersrand)	79

LETTERS TO NATURE

Physical Sciences

γ -ray astronomy—Ionospheric effects of cosmic bursts—BROWN (Los Alamos)	83
Solar system—Structure of terrestrial planets—LYTTLETON (Cambridge)	84
—Reply—BULLEN (Sydney)	85
Geodesy—Refining Earth's pear shape—KING-HELE and COOK (RAE, Farnborough)	86
Seismology—Microearthquake study of Mid-Atlantic Ridge—REID (California, San Diego) and MACDONALD (Woods Hole and MIT)	88
Crystallography—Location of hydrogen atoms in ADP by powder diffraction—HEWAT (Harwell)	90

Biological Sciences

Interferon—Inhibits B lymphocyte expression in response to primary antigen stimulation—CHESTER (Stanford), PAUCKER (Medical College of Pennsylvania) and MERIGAN (Stanford)	92
RNA precursors—Changes in the incorporation of different RNA precursors into the maternal liver during pregnancy—HAYASHI and MacFARLANE (Pittsburgh School of Medicine)	94
Natural selection—Effect of slightly deleterious mutant substitutions on evolution—OHTA (National Institute of Genetics, Mishima)	96

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 61 to 65

Cell

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of cells and their viruses

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	Page		Page
Cancer —Antitumour activity of iodine in acidic medium with calcium—VOLTII, PIHA, PALVA (Oulu, Finland) and ALAVAIIKKO (Kokkola, Finland)	98	Malnutrition and Retarded Human Development, S. L. Manocha (D. F. HOLLINGSWORTH)	108
Vitamin D —Induction of synthesis of mRNA for calcium binding protein—EMTAGE, LAWSON and KODICEK (Dunn Nutritional Laboratory and MRC, Cambridge)	100	Boranes in Organic Chemistry, Herbert C. Brown (M. F. LAPPERT)	109
Tumours —Abrogation of lymphocyte trapping by ascitic tumours—FROST and LANCE (Clinical Research Centre, Harrow)	101	The Generation of Subcellular Structures, R. Markham, J. B. Bancroft, D. R. Davies, D. A. Hopwood and R. W. Horne (M. R. POLLOCK)	109
Histone kinases —New enzyme in nuclei of rat tissues—SMITH, BRUEGGER, HALPERN and SMITH (California, Los Angeles)	103	Guide for Safety in the Chemical Laboratory, Manufacturing Chemists Association (PETER FARAGO)	109
Sickle cell disease —Elevated levels of calcium in the erythrocytes—EATON, SKELTON, SWOFFORD, KOLPIN and JACOB (Minnesota)	105	Elementary Processes at High Energy, 1970 International School for Subnuclear Physics, A. Zichichi (editor) (R. H. DALITZ)	110
BOOK REVIEWS		CORRESPONDENCE	
Palaeoethnobotany: The Prehistoric Food Plants of the Near East and Europe, Jane M. Renfrew (A. R. CLAPHAM)	107	CO ₂ Pollution of the Sea (G. A. Wood)/Are Conferences Necessary? (R. Cooper)	111
Electrical Phenomena in the Heart, Walmor C. De Mello (editor) (O. F. HUTTER)	108	Obituary—A. G. Sharov	111
		Announcements—University News/Appointments/Miscellaneous/International Meetings	112

Next Monday's issue will include

- QSOs**—Redshift problem discussed—BURBIDGE (California, San Diego)
- Weber events**—Significance of sidereal period—SHAHAM (Illinois)
- Geophysics**—Magnetisation and tectonics of Grenville Province—BUCHAN and DUNLOP (Toronto)

Next Wednesday's issue will include

- RNA conformation**—Improved estimation of secondary structure in ribonucleic acids—TINOCO, BORER, DENGLE, LEVINE (California, Berkeley), UHLENBECK (Illinois), CROTHERS and GRALLA (Yale)
- Membrane structure**—Structural changes in sarcoplasmic reticulum membrane induced by SH reagents—DUPONT and HASSELBACH (Max-Planck Institute, Heidelberg)
- Cholesterol**—Regulation of rat liver β -hydroxy- β -methylglutaryl-CoA reductase activity—HIGGINS and RUDNEY (Cincinnati)
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The Ethiopian Calamity

THE attractions of Ethiopia to the tourist are substantial. Daily flights from Europe to Addis Ababa make it an easily accessible country. The last leg of the journey is from Asmara, in Eritrea, to Addis. Beneath this spectacular flight lie the Ethiopian highlands and the extraordinary churches at Lalibela, hewn directly out of the rock. Beneath the flight path and to the east of it, also lie tens of thousands of dead, in regions now gripped by as bad a famine as relief workers have ever encountered.

The region worst affected lies between Makale in Tigre and Dessie in Wallo. In this area there is one rainy period a year, from June until early September; this is the summer monsoon season. As Winstanley pointed out in *Nature* (245, 190; 1973), mean summer rainfall has recently declined from 165 to 100 mm per year for a set of stations across the Southern Sahara to Khartoum. It is this rainfall which makes much of the middle levels (up to 1,500 m) of Ethiopia suitable for cultivation and grazing, and it is its failure that has led to the famine.

In 1972, crops such as millet, maize and sorghum could not be planted. Thus by September 1972 the tragedy had begun. Between then and May 1973, 80% of the cattle were lost and there were smaller losses of camels. In May, the international organisations working in Ethiopia switched their efforts from development to relief and a plea went to the UN World Food Programme for assistance. Aid did not materialise from this source for several months and meanwhile the Ethiopian government, with organisations such as Oxfam and Christian Aid, were trying to cope in a region in which adequate roads were practically non-existent. For several months, however, the world at large was allowed to know nothing as the government kept a very low profile. Meanwhile the Sahelian countries were forthcoming about their similar troubles and received early aid. This cover-up persisted until Ethiopian students in Addis heard of the disaster and approached Mr Jonathan Dimbleby. The result was the powerful film shown on Thames Television two weeks ago. Mr Dimbleby has since broadcast an appeal for financial support for a relief programme which seems destined to continue for at least a year. And still the full extent of the famine is unknown, because Tigre province includes inaccessible villages in which it is feared more may have died.

What can be done about this terrible disaster? There is, of course, a continuing need for money to support the concerted actions of the voluntary organisations. There is also a need for technical, particularly medical, personnel to do a short tour of duty in the area. There are, however, many broader issues to face. This catastrophe had been foreseeable since September 1972 and yet nothing was done when there was still time. Further, the severe drought conditions south of the Sahara this year did not seem to alert anyone to the possibility that Ethiopia was having similar problems. One cannot be sure, even now, that all affected regions have been identified—is southern

Sudan free of trouble, for instance? The situation in Ethiopia here and now could have been surmised both by earlier observations in Ethiopia and present observations elsewhere. There is even a large American military communications facility within 150 miles of the region. Yet it needed a television programme to alert the outside world.

No doubt there will be proposals for more technology to improve our understanding of climate, more satellites to keep watch, more equipment in the field, better drought-resistant plants. One cannot but hope that science will provide some future comfort. The central issue, however, has no technological solution; it is a social and political problem and is seen in a most exposed form in Ethiopia. It springs from pride in external relationships and a lack of understanding in internal ones. The ruling race are the Shoans, highlanders centred on Addis, and even a sympathetic observer describes them as "proud, aloof, self-sufficient". It is unlikely that they understand the ways of the herdsmen and farmers in Wallo and Tigre. They certainly know little of the character of the nomadic Danakil people. The present situation finds the central government ill-prepared mentally, however much aid they may distribute. Worse, there has clearly been a great unwillingness to allow external publicity and this can only be attributed to misplaced pride and a fear of loss of tourist income.

It is obvious that as long as governments all over the world are too proud to think beyond national solutions to human problems, and relief agencies are hamstrung by political sensitivities, such tragedies will occur with regularity.

100 Years Ago



THE following awards have been made by the French Geographical Society :—2,000 francs to M. Dourniaux-Dupéré, who has just set out for Timbuctoo; this gentleman has also received a similar sum from the Minister of Public Instruction; 2,000 fr. to M. Francis Garnier, to aid him in his explorations along the Blue River in China, and which have Yun-nan and Tibet for their objects; 1,500 fr. to MM. Marche and Compiègne, who have already proceeded a considerable distance along the course of the Ogowe with the design of penetrating as far as the great African lakes, and joining Livingstone.

From *Nature*, 9, 33, November 13, 1873.

The Problem of Compensation for Antenatal Injuries

Dr R. G. Edwards of the University of Cambridge puts forward some personal opinions arising from a discussion at the Institute of Advanced Legal Studies on aspects of fair compensation for injuries sustained before birth.

I WISH to discuss certain points about Working Paper No. 47 of the Law Commission (January 1973) on injuries to unborn children. This proposes statute law for liveborn children suffering antenatal injury to claim damages where negligence of another person can be proven. The concern by lawyers for children with handicaps should be widely welcomed. I have some misgivings, however, about the nature of the proposals, for the correct approach to helping these children should not involve compensation by proof of fault. My doubts arise on several scores:

- The situation created by changes in drug testing methods since thalidomide;
- Difficulty in deciding the causes of many prenatal injuries;
- The possibly complex social consequences arising from legislation, for parents, offspring and doctors;
- The potential unfairness of such legislation to children with birth defects unable to claim compensation under it.

I would also like to explore the possibilities of other approaches to the fair treatment of injuries to foetuses before livebirth.

Causes of birth defects

Many children are born handicapped to varying degrees, and estimates vary between two and six per cent, partly through differing opinions on the nature of the anomalies, and partly because some are manifest long after birth. Some of these handicaps arise genetically, and others through the effects of teratogens during pregnancy. Often there are difficulties in separating the relative contribution of genetic and environmental effects, and interactions between them, and in many cases of birth defects the parents or doctor in attendance will have contributed, accidentally or otherwise.

Teratogens are evidently the main concern of the Commission, and deserve an opening comment. There are practically no guidelines at present in United Kingdom law on compensation for such injury. The unsatisfactory nature of this situation has been highlighted by the recent social debates on compensation for thalidomide children. The funds awarded to these children are obviously a wonderful uplift to them and their parents, and their financial difficulties, at least, should be over. Yet, as well as

the manufacturers, many people and agencies, including the Health Service, were involved in events leading to the thalidomide situation. Responsibilities for drug testing in pregnant animals and for the nature of the tests were diffuse or unrecognised, and fell largely on the manufacturers. This situation has changed since thalidomide, for the governmental Committee on Safety of Medicines now tests new drugs and issues recommendations. In my view, legislation will have to accept this new situation and adapt to it, for a great deal of responsibility for any foetal injury through drugs taken by the mother must now fall on this committee.

My next reservation about the proposed legislation concerns the difficulty in deciding the cause of many congenital defects, for a handicap arising genetically could be mistakenly attributed to exposure to drugs or trauma during pregnancy. There must be many pregnant women carrying a foetus with a genetic defect who are exposed to a potential teratogenic agent, and many misinterpretations in deciding the cause of damage to the child. Indeed, some have already arisen, as judged by some cases in common law. A child was awarded damages for 'imbecile mongolism', judged to arise through injury involving the mother at one month of pregnancy¹. From what we know today about mongolism (trisomy-21), these damages must be unjustified; either a medical misdiagnosis or a miscarriage of justice has occurred, for the chance of a succession of simultaneous chromosomal changes in the cells of a 1-month-old foetus can almost certainly be totally excluded. Similar doubts about the justice of the award were voiced by a dissenting judge in this case. Many of the examples given in the Commission's report appear to be questionable, for club feet and epilepsy evidently have a distinct genetic component²⁻⁴.

Such difficulties seem bound to arise in analyses of the effects of the teratogenic agents quoted in the report; drugs, trauma, X rays and disease. Teratogens usually exert fairly specific effects. One criterion adopted by teratologists is that the type of damage caused must be typical of the agent and of the time during pregnancy at which it was administered. Clear proof of the

effect of teratogenic agents in man will be difficult to obtain; perhaps they could be shown to induce similar anomalies in animal foetuses, but even so the relevance of these observations to man could be questioned.

Trauma is seldom discussed as an agent causing foetal anomalies—foetal death is a more likely consequence. Hardly a case of foetal deformity due to trauma is considered in textbooks, except very recently⁵. The evidence available is shown to be extremely limited indeed; a direct blow to the foetus might inflict damage without death, but clear examples are very hard to prove. Some fairly bizarre examples might arise, such as anoxia following the death of the mother before Caesarean delivery, or accidental damage during surgery, but these hardly seem worth such weight of legislation. Radiation damage is now well recognised, and while mistakes can arise through negligence the best solution to an accidental heavy exposure to X rays might be to abort.

Disease raises very difficult problems. Since it properly includes the effects of German measles and other teratogenic viruses, are there to be penalties for spreading these conditions in a community? The social problems could become even more complex, for foetal handicaps arising from this source would probably be due to parental negligence, so that questions of actions in law by children against their parents would arise, as I shall discuss below. There have been rare cases where the use of contaminated blood⁶ or semen by doctors has led to claims in common law by the deformed child.

Problems in claiming compensation

Much of the proposed legislation could involve claims by children against parents, for example, in the case of congenital syphilis, and once begun such claims could spread to many other situations. Some habits of the mother can impair foetal growth: low birth weights and anomalies in offspring have been reported if the mother smokes or drinks alcohol during pregnancy. There could be grounds for action by children against parents for genetic defects; for example, should a second child have deformities similar to those in an earlier child then the parents might be accused of negligence in the second conception. Claims could even be brought by children for a defective genetic constitution, bastardy or being born half-caste. If the suggestion that these situations could lead to litigation appears to be extreme, let me offer the

defence that these topics have already been discussed elsewhere and some common law cases have actually been heard in court already⁶. The potential upsets to family and social life resulting from numerous claims against parents by children led one court⁷ to decide in favour of the parents even though they were sympathetic to the child's claim, a decision soundly criticised by one legal authority who insisted that such cases should be heard, for if there is a damage then justice must be done⁸. Arguments raised in some related cases led, for example, to justices being compelled to debate the meaning of existence when a child born defective as a result of German measles brought an action against the doctor for wrongful birth⁹.

Further difficult issues may appear with reference to claims arising from agents or acts applied before conception occurred. As far as I am aware, there is no clear evidence, even in animals, to show that specific damage to gametic cells before conception can induce anomaly manifest after birth, with the possible exception of chromosomal imbalance and rare genetic changes. With respect to teratogens, the available evidence shows that eggs and embryos are highly resistant to induced malformation shortly before and after fertilisation. Legislation would therefore be effectively restricted to a few cases. There is also a broader point to be considered concerning the role of doctors and others in helping to establish conception in infertile patients and this is, of course, a field in which I have a direct interest. Many children are now being born after the use of artificial insemination with donor semen, the use of hormones to induce ovulation and other methods of alleviating infertility. Causes for legal action of the liveborn child against the doctor could arise under these conditions, for example, on the choice of the semen donor for AID. A recent report from Germany has implied that children conceived by AID have the right to know the name of their natural father, and doctors refusing to divulge it or creating difficulties in establishing his identity by mixing the semen from several men could be held in law as withholding natural rights from the child¹⁰. Children might be encouraged by legislation to sue the doctor who helped to give life, a possibility more likely than their claiming against parents since the doctor possesses financial resources outside the family. Vital treatment for patients might be withheld because doctors were unsure of their legal position.

These considerations indicate that great care must be taken in framing legislation to cover injury to unborn children. The actual wording of the legislation could lead to further problems. A girl born in 1969 in Vancouver

with defects identical to those of 'thalidomide' children was excluded from many of the benefits of legislation for these children because the real cause of her malformations was unknown (R. B. Lowry, personal communication). I doubt too that the award of damages based on fault to such children is the right or best way to help them in life, with the attendant disadvantages of legal action by a parent or third party sufficiently determined to carry the case through. The legislation would help too few of the children who are afflicted, and probably result in a minority of them obtaining large sums of money while the others depend on state or other benefits. Nor is legislation likely to act as a deterrent, because most injuries will arise accidentally and not with forethought. Granting the right to liveborn children to sue for uterine damage could lead not only to cases of Wrongful Life, but to the more complicated problem of Wrongful Death, in which stillborn foetuses can be the subject of claims, or even have claims brought on their behalf^{10,11}. When these daunting aspects are related to the problems outlined above there would seem to be good cause to search for another method of dealing with foetal injury.

Possible alternatives

An alternative approach can be discerned in existing institutions. The Pearson Commission on Civil Liability and Compensation for Personal Injury has recently been established to consider how compensation should best be payable and financed in respect of death or personal injury arising in various ways, and it will consider antenatal injury. Legislation has already been passed in the United Kingdom to help disabled people (including disabled children) although there are some grounds to believe that the legislation is not being satisfactorily implemented¹². This statute should be fully implemented to provide generous rehabilitation facilities by the state to all children with congenital injuries, whatever the nature of their origin, and so increase the effectiveness of the measures now available. The statutory provisions should be sufficiently generous to take care at least of the medical and social urgencies associated with physical handicap, education, vocational training and employment, and protect the parents as far as possible from suffering and financial loss; some countries have already taken such steps¹³. An important aspect in financing could be to establish a system of "liability without fault" for antenatal injuries, such as the Pearson Commission is considering. Insurance or other systems would be needed to raise funds.

A further lead can be gleaned from the work of the Committee on Safety of Medicines which has statutory authority to oversee and control new

developments in its field. This or another committee could be given wider authority to extend current schemes, mostly local, to monitor the incidence and type of birth defects (chronically sick and disabled persons, including newborns, are now registered by local authorities under the Chronically Sick and Disabled Persons Act (1970)¹⁴). It could also take some of the responsibility for advising and helping doctors and others in making decisions about the value of new methods, and undertake some responsibility to oversee the rights of foetuses. A danger of such a committee might be delay in the application of new methods, unless such developments were excluded from the scope of its deliberations. Within this framework, some organisation might be created to oversee conditions in this field, if necessary having the right to bring actions for negligence against offending parties, and providing legal and medical help where needed. In a different context, compensation for injuries arising to adults through criminal or other action can be awarded by a board, and guardians for unborn children have been legally appointed in the past⁶. I do not know if such compensation could be conferred within our legal situation, although funds can be provided in various ways, for instance, by Royal Prerogative exercised by the Home Secretary in the case of injuries through criminal action.

Ultimately, expenditure of public funds would need legislation, and suitable steps would be required to provide any such committee with appropriate authority. In the meantime, exploratory steps could be taken, or some other systems proposed, in order to avoid many of the pitfalls accompanying legal questions concerning parents, children and other parties, and yet give maximum support to those needing it most—the children afflicted at birth.

¹ Sinkler v. Neale, 401, Pa. 267, 164 A 2d 93 (1960).

² Carter, C., & Morton, E., in *Congenital Malformations* (Excerpta Medica, 1969).

³ Kalter, H., *Teratology of the Central Nervous System* (Chicago, 1968).

⁴ Wilson, J. G., *Environment and Birth Defects* (Academic Press, New York and London, in the press).

⁵ Bundesgericht 20 XII 1952, *Juristenzeitung*, 307 (1953).

⁶ Tedeschi, G., *Israel Law Review*, 1, 513 (1966).

⁷ Zepeda v. Zepeda, 4, 111 App. 2d 240, 190 NE 2d 849.

⁸ Gleitman v. Cosgrove, 49 NJ 22, 227 A 2d 689 (1967).

⁹ *Frankfurter Allgemeine Zeitung*, January 3, 1973.

¹⁰ Fowler v. Woodward, 138 S.E. 2d 42 (S. Car., 1964).

¹¹ Quinn, A. J., and Griffin, J. A., *The Jurist*, 31, 577 (1971).

¹² Morris, A., *The Times*, June 19, 1973.

¹³ Lind, J., in *Congenital Malformations* (Excerpta Medica, 1969).

¹⁴ Morris, A., & Butler, A., *No Feet to Drag* (Sidgwick & Jackson, London, 1972).

NEWS

Canadian Societies seek More Involvement

from a Correspondent

THE Royal Society of Canada, together with others among Canada's 119 engineering, scientific and technological societies, has been absorbed recently in a searching re-evaluation of its functions and its proper role. One sign of the society's attempts to move with the times was its sponsorship last month of a symposium on energy resources. Some observers in Ottawa are wondering whether the symposium reinforced, rather than changed, the society's public image as an ultra-conservative club for senior scientists, as the meeting was almost entirely devoid of either controversy or confrontation. It is worth recapitulating some of the background to this attempt at increased involvement.

Last December the Science Council published a study* which recommended a more active role for scientific societies in dealing with the implications of science and technology for society. It was also proposed that the federal government should establish a 'Canadian House of Science, Engineering and Technology' to provide the societies with offices and meeting space for their secretariats.

Written by Professor A. S. West, an entomologist from Queen's University, the study also noted the following difficulties facing most Canadian scientific societies:

- They are small and compete with larger counterparts in the United States;
- They have low fees and small incomes, yet must cope with the expense of bilingualism;
- Their young scientists are too little involved and often have a poorly developed social conscience.

Professor West did his study under contract from the Science Council of Canada through an organisation known as SCITEC (the Association of the Scientific, Engineering and Technological Community of Canada). SCITEC was formed in 1970 in response to the complaint of members of the Senate special committee on science policy (the Lamontagne Committee, see *Nature*, 245, 406; 1973) that they could not find a single voice to speak for all of Canadian science. It has since abandoned any pretence of fulfilling such an oracular function, but is now the principal contender, together with the Royal Society, for leadership among Canadian scientific societies.

The two societies are quite different

in purpose and structure. The Royal Society is the Canadian equivalent of an academy of science, but SCITEC is somewhat analogous to the British or American Associations for the Advancement of Science. Both groups claim, however, some similar functions. One of these is to increase public understanding of scientific issues; SCITEC itself had already held a symposium on the social and economic implications of the energy situation.

The report of the Lamontagne Committee proposed that the two organisations should not compete but cooperate, by defining and dividing their functions. "The Royal Society," it said, "with its reservoir of scholarship represented by its fellows and scientific panels could concentrate its national activities on the use of science for policy—on scientific and technological studies dealing with Canadian issues. SCITEC, as an overall spokesman for the engineering, scientific and technological societies, could specialise on policies for science and technology—on broad issues concerning scientists, engineers, and technologists in the exercise of their professions."

The Royal Society's latest symposium, however, seems to some to cast doubt on the claim of its president of last year, Professor Tuzo Wilson, that the organisation is being revitalised. For although the subject matter (energy) was highly topical, the approach and the choice of

speakers and subjects seemed conventional and the papers added nothing new to an already much-debated problem. What little discussion was allowed, was conducted by means of written questions; a practice that brought a formal complaint from some of the younger members of the audience.

There were some good things. The society took unusual steps to publicise the venture and had a good attendance as a result (some 300). The review papers provided a mass of information. And three of the thirty-five speakers departed from the predominant theme—how to increase the energy supply—by proposing that perhaps what is needed is a whole new policy of moderation of life styles to slow down the rate of increase in the use of energy. One of the three was former chairman of the Economic Council of Canada, John J. Deutsch.

In his report, Professor West spoke of the need of a major overall co-ordinating organisation to increase the involvement of Canadian scientific societies, and he quoted an unnamed scientist as saying it must be "of such stature and articulation that the public will accept its pronouncements on the same plane at least as those of the Science Council."

The impression remains that, in spite of recent attempts, neither society has yet succeeded in fulfilling that role.

MEDICAL JURISPRUDENCE

Transplants and Murder

by our Washington Correspondent

A MURDER trial which is to open in California on December 18 will be the venue for a legal battle over the precise definition of death, and the outcome will have significant implications for transplant surgery. At the centre of the trial is Andrew D. Lyons, who is accused of shooting Samuel Moore, a 29-year-old California man, in the head on September 10, 1973. On September 12 Mr Moore's brain showed no signs of electrical activity, he was unable to breathe, and did not respond to stimulation. He was then pronounced "neurologically dead", and his heart was used in a transplant operation performed by Dr Norman Shumway, a Stanford heart surgeon who has performed some 65 transplants; 23 of his patients are still surviving.

Californian law allows transplants to be performed provided that the donor has been pronounced dead, but no pre-

cise legal definition of death is given. In this case, according to the *New York Times*, Moore's wife and mother had given permission for the transplant, Moore was pronounced dead on the grounds of a lack of cortical activity, and his heart was removed while still beating. Clearly, the concept of brain death is going to play a large part in the trial. There is, however, one close parallel case in American legal history. Last year, a team of surgeons from the Medical College of Virginia was acquitted of a charge of killing a 56-year-old black man to use his heart in a transplant operation. In that case the donor suffered brain damage as the result of a fall, and he was pronounced dead when an electroencephalogram showed no signs of electrical activity in the brain. His heart was subsequently removed, while still beating, and used in the first heart transplant carried out in Virginia. The jury in the trial had little difficulty in deciding that the donor was legally dead when his heart was removed, and the doctors were acquitted.

* *National Engineering, Scientific and Technological Societies of Canada*, A. S. West, Science Council Special Study No. 25.

Short Notes

Le Ballon Rouge

THE first part of a new Franco-Soviet drift-balloon project, to investigate high altitude phenomena at Arctic latitudes, will soon begin with the launching of a balloon from a test site in Sweden. The experiment, called "grebenka" (comb), is intended to monitor charged particles and associated phenomena during the aurora borealis, and will consist of two series of balloon flights, the first in winter 1973-74 and the second a year later. The flights will be at an estimated altitude of 35 to 45 km, and due to the strong westerly prevailing winds are expected to proceed eastwards from Sweden over the northern islands of the Ural ridge for a distance of some 2,000 km.

According to *Pravda* (October 31, 1973) the balloon is to be tracked throughout by radar and the data gathered are to be transmitted to the ground station and recorded there for subsequent analysis—a somewhat surprising procedure, since it is explicitly stated that one of the objects of grebenka is to monitor those conditions in which radio communications break down.

Skylab Launch Date

THE launch of the third and final crew of Skylab has now been scheduled for November 10. This is earlier than some astronomers had hoped, and it seems that Skylab will, after all, be unmanned for part of the period in January when Comet Kohoutek is expected to be at its most spectacular. But according to NASA "consumables will be closely husbanded to keep open an option to extend the final mission to about 70 days". Kohoutek will reach perihelion on December 28, and a "standard" 56 day mission would terminate on January 6. But if the mission does run until January 20, 1974, or thereabouts, there would be opportunities for studying ice and snow distributions in the northern hemisphere, and the start of the growing season, as well as making further observations of Kohoutek. The two earlier Skylab missions lasted for 28 and 59 days.

Russian Nuclear Activity

THREE underground nuclear explosions were fired on October 26 and 27 in the Soviet Union in the most vigorous burst of activity ever recorded. One shot was in the normal testing ground near Semipalatinsk, and a second was on the Arctic island of Novaya Zemlya. This latter was the largest ever fired underground in the Soviet Union and was comparable in yield to the Cannikin blast in the Aleutians in 1971. Several aftershocks were recorded from the event. The largest had a magnitude of 4.6. This is the first occasion on which

aftershocks of Soviet tests have been reported. The third shot was in the Urals region and was in all probability for peaceful purposes. Soviet Plowshare activity in the last two years has been at the high level of between ten and twenty shots each year.

Winning Sargassum War

ATTEMPTS to clear the Japanese seaweed *Sargassum muticum* from the Isle of Wight and Portsmouth harbour are proving successful. The weed is being collected fortnightly and the majority of fronds are only 20 to 30 centimetres long—the length to which they grow in about a fortnight.

As yet a committee formed by local authorities with representation from the Nature Conservancy the Ministry of Agriculture, Fisheries and Food, the local river authorities and the Natural Environment Research Council (NERC) has still to meet to decide if money is to be allocated to help with the eradication.

To date the £500 spent on clearing the weed has all come from Portsmouth Polytechnic, the Nature Conservancy and a local trust, with studies of the seaweed's behaviour being financed by NERC. Local authorities have still to make a contribution.

Dr Gareth Jones, of Portsmouth Polytechnic, who has been organising the eradication programme says that "at the moment, there is no real threat as we are digging the seaweed up, but come next spring there very well could be a problem. It is under control now; it does not necessarily mean that it will be by then".

To keep the weed—which grows at the alarming rate of 1 to 2 centimetres a day and which could create a hazard for shipping, cover oyster beds and foul beaches—under control, a full-time appointment is needed. To ensure that the weed does not become established in Britain the young plants that are springing up will have to be removed regularly for the next 2 or 3 years.

Centrifuge Setback

THE United States gas centrifuge programme for enriching uranium received a severe setback on October 20, when a model centrifuge was destroyed in an accident at the Oak Ridge plant in Tennessee. The accident, which was made public by the Atomic Energy Commission last week, occurred when an advanced model centrifuge failed at high speed, damaging several other units and releasing 4 ounces of uranium hexafluoride. By good chance, the accident occurred on a Saturday, when few people were in the building, and nobody was hurt. What effect the accident will have on the programme remains to be seen, and the AEC is not yet prepared to give many details away. An investigation is under way, however, and its

findings will determine the extent of the adjustments, if any, that will have to be made in the design and operation of its other centrifuges.

USGS Gets the Lot

THE United States Geological Survey has inherited all the seismological, geomagnetic and earthquake research programmes from the National Oceanic and Atmospheric Administration (NOAA). Prime object of the transfer is to save money by consolidating the Geological Survey's extensive activities in Earth sciences with those of NOAA, and to cut down on the duplication of effort which has been going on, particularly along the San Andreas Fault. The first stage of the transfer took place in June, when NOAA's Earthquake Mechanisms Laboratory in San Francisco was merged with the Geological Survey's National Center for Earthquake Research in Menlo Park. The second stage, announced last week, completes the transfer of NOAA's entire programme, including management of the Worldwide Standard Seismograph Network, the National Earthquake Information Service and all the seismological observatories except for three needed for the tsunami warning system. As far as the first stage of the transfer is concerned, it seems that difficulties have arisen because the two laboratories were doing parallel work, and redundancies are expected.

Comet Kohoutek Limited

Two London businessmen have come up with the bright idea of registering the name 'Comet Kohoutek' for business purposes. Operating as Comet Kohoutek Limited, they are at present negotiating with "a number of national advertisers" in Britain intent on using the comet to promote such items as toys and fireworks. A spokesman for the company said this week that one national newspaper has already come to an arrangement with Comet Kohoutek Ltd about use of the name, but he could not give any details before the promotion gets under way. Members of the scientific and journalistic communities will no doubt be relieved to learn that they can use the name Comet Kohoutek in describing the comet without fear of prosecution; but anyone who is based in Britain and wants to market, say, a new drink called 'Kohoutek—the fizz with a wizz' will have to pay for the privilege. Comet Kohoutek Ltd operates from 11 Ranmore Court, Catherine Road, Surbiton, Surrey KT6 4HE.

No Comment

"It will add considerably to our inadequate knowledge in the ill-documented field of . . ."—Book advertisement in a recent issue of *Nature*.

NEWS AND VIEWS

Hot Spots on X-ray Sources

THE study of X-ray sources is one of the great success stories of present-day astrophysics. For objects like Cen X-3 or Her X-1 it is possible to build up a model which is based, almost entirely, on qualitative arguments. Thus the X-ray observations of these sources show short period fluctuations in brightness, on a time scale of seconds. No simple astronomical object can oscillate or rotate as fast as this unless it is considerably denser than a white dwarf. The next densest type of object is a neutron star, and so the first qualitative conclusion is that the X-ray emission comes from neutron stars (at least).

Superposed on the short period fluctuations there are longer period variations, very reminiscent of those seen in eclipsing binaries. Optical astronomers have long been very fond of such close binaries, for their detailed observation readily permits the determination of interesting physical parameters, such as the masses and the radii of the partners, and their distance apart. More than that, it has been realized in recent years that the close proximity of one star to another may lead to great perturbations in the behaviour of one or both members of the pair. The most important of these effects is a strong tidal distortion, which allows mass to stream out of one star and into the other.

These ideas have a counterpart in the case of the X-ray sources. The generally accepted model has it that the binary consists of a rather ill-matched pair of stars. The primary star is large and diffuse; once in each period it eclipses the secondary, which is very compact, and which also emits the X rays. Because the secondary emits so much energy (in the form of X rays) it will cause a considerable modification in the properties of the atmosphere of the primary. It is quite possible that most of the radiation from the primary is really derived from energy generated on the X-ray source. It is equally likely that the uneven heating caused by the X-ray source will lead to the loss of mass from the outer layers of the primary.

Here is a crucial point in the whole description, for it is this very gas, which the X-ray source extracts from the primary, that finally falls on the neutron star and provides the energy for the X-ray emission. The energetics of the process can be quite satisfactorily understood. It requires of the order 10^{15} erg of energy to pull one gram of matter off the surface of the primary. But about 10^{20} erg can be recovered for each gram that falls on the neutron star. Once the pump is primed it should go on running quite satisfactorily even if only a small fraction of the gas finds its way to the neutron star, and even if most of the X-ray energy escapes into space.

Now how does this gas get down onto the surface of the neutron star? From the theory of pulsars one knows that neutron stars often have strong magnetic fields. In the case of the X-ray source the infalling material, which will of course be highly ionized, must be guided down to the surface along the lines of force of the magnetic field. The outermost lines of force in the field are those which originate at the magnetic poles.

So the gas falls down a pair of 'funnels', each of which terminates at a magnetic pole. This is where the potential energy released in the fall is turned into X rays. As the X-ray source turns the hot spot(s) can intermittently be seen. Hence the pulsation of the source.

This is indeed a persuasive picture, but it is based on more hand-waving than even an astrophysicist is likely to be used to. Nobody can yet describe exactly how the uneven heating by the X-ray source affects the thermal balance of the atmosphere of the primary, nor how much mass loss results from it. Nobody can yet say how the circumstellar plasma will interact with the low frequency radiation from the rotating neutron star. Finally, nobody can yet give a hydromagnetic description of the process by which the neutron star captures the plasma. But at least a start has been made on a description of the last stages of the infall.

In an article in last Monday's issue of *Nature Physical Science* (246, 1; 1973) Davidson discusses the mechanics of the plasma flow in the region just above the magnetic poles. Here the infalling gas is constrained to move along the lines of force, which are almost rigid because the magnetic field is so strong. As it comes close to the surface, the gas is decelerated by radiation pressure. But because it is slowed down, it must lose energy, which it gives up to the radiation field, thereby adding to the radiation pressure. It turns out that the radiation cannot escape upwards against the gas flow. Instead it leaks away through the sides of the funnel.

Comparison shows that this relatively simple sequence of ideas can be brought into good agreement with observation. A set of quite homely parameters describes the mound of gas where the X rays are produced. It is about as high as the Post Office Tower, covers an area somewhat smaller than Hyde Park, and the mass per unit area in the mound is about the same as the mass per unit area in the Earth's atmosphere.

It seems out of the question that these predictions will ever be verified by direct observation. On the other hand, it is unlikely that anyone will ever seriously challenge these conclusions, except perhaps in some minor way.

F. D. K.

Lymphocyte Trapping

CELLULAR immunologists have been so enthusiastic in their pursuit of knowledge that they have described many phenomena of which, at present, the biological significance is uncertain. Allogeneic inhibition, for example, which related to various situations in which foreignness of environment was apparently inhibitory to a wide variety of cell populations, was popular a few years ago. Nobody knew whether it was significant in relation to the growth of a tumour, or a kidney allograft, but it was, and presumably still is, an interesting phenomenon. Perhaps the discovery of allophenic mice in which genetically very disparate cells seem to exist in cheek and jowl in perfect

harmony presaged the decline from favour of the notion of allogeneic inhibition. Lymphocyte trapping, the subject of a communication by Frost and Lance on page 101 of this issue of *Nature*, is similarly a phenomenon widely thought about but of which the biological significance is unclear.

In earlier papers Lance and his colleagues have described how, when mice are injected with ^{51}Cr -labelled syngeneic lymphocytes during an immune response, the label appears preferentially in the responding lymphoid organ. Other immunologists have shown a small drop in lymphocyte output from lymphoid organs in the early stages following antigenic stimulus, and it seemed to Lance and his colleagues reasonable to suppose that during an immune response there were alterations in the flow of lymphocytes through the responding organ such that more cells were, in the Lance terminology, trapped. It has been found that although trapping can occur during an immune response, the mechanism is more or less independent of the immunological status of the organism in which trapping is demonstrated.

In their new paper Frost and Lance describe how trapping is much reduced in both the spleen and lymph nodes during a response to antigen in mice, which also carry certain transplanted ascites tumours. Ascitic fluid injected into non-tumour bearing recipients had a similar depressing effect on the trapping system. As it was shown in other experiments that the same tumours growing in a solid condition failed to alter the capacity to trap—which indeed was augmented in lymph nodes draining the site of implantation of the tumour—the authors could not argue that malignancy *per se* was having an immunosuppressive effect. Nevertheless, they postulate that part of the immunosuppression sometimes found in advanced cases of malignancy could be due to failure of trapping.

It will be of considerable interest to find out whether the mice with ascitic tumours had similar factors in their serum to those found in shock plasma which can inhibit some of the activities of the reticuloendothelial system. It could be that trapping is a manifestation of stimulation of the macrophages and that in various 'stress' situations trapping is reduced because of partial failure of excitation of macrophages.

From a Correspondent

EPIDEMIOLOGY

Sexual Transmission of Hepatitis B

from our Medical Virology Correspondent

THE epidemiological concepts of hepatitis B infection have recently undergone a significant change. The demonstration that the hepatitis B agent is infective by mouth and the finding that the infection is endemic in closed institutions, the prevalence of infection in adults in urban communities, the carrier rate and age distribution of hepatitis B antigen in different geographical regions and the relatively high incidence in poor socioeconomic environments, have altered the epidemiological dogma that hepatitis B is spread exclusively by blood and blood products through the direct parenteral or percutaneous route. Some evidence is now also available for the transmission of hepatitis B by intimate personal contact and possibly by the venereal route.

In 1971, Hersh and colleagues (*New Engl. J. Med.*, **285**, 1363) presented the case history of six patients with hepatitis B infection. Although the precise mode of transmission from a man to his close female companion or companions was not clearly defined, a non-percu-

taneous route was strongly implicated. The first patient developed hepatitis 3 months after blood transfusion, hepatitis B antigen persisted in his blood and 3 months later his wife developed antigen-positive infection. The second patient was a drug addict who contracted acute hepatitis B; his wife, who was not an addict, developed hepatitis without jaundice 4 months later and the antigen was detected transiently in her serum. The third patient suffered from hepatitis and his girl friend developed a similar illness 3 months later. The fourth patient was a technician working in a renal dialysis unit and hepatitis B antigen was detected in his serum during routine examination. Three of his intimate female contacts developed acute hepatitis B infection. Another patient developed acute hepatitis B; her husband had chronic hepatitis and the antigen was repeatedly found in his serum. The sixth patient in this series was a drug addict, who died of acute fulminant hepatitis. His girl friend, who did not take drugs, suffered from acute hepatitis 2 months later.

CEA-like Substance on Erythrocyte Membranes

IN 1965 Gold and Freedman described an antigen which was thought to be specific for human tumours and foetal tissues of endodermal origin. Called carcinoembryonic antigen (CEA), it was a finding of potentially great importance. But it was not until about four years later, when the first CEA radioimmunoassays were reported, that the CEA story really began to interest the scientific community. Such methods suddenly gave rise to the possibility of being able to perform early screenings for the deadly colonic carcinomas, at a time when the disease would not yet be clinically apparent. Sadly, more recent experience has shown that this hope was over-optimistic; for colonic CEA, or substances cross-reactive with it, has been detected by various methods to occur in the urine, plasma, or faeces of patients with both neoplastic and non-neoplastic (usually inflammatory or regenerative) disorders, and even, albeit in much smaller amounts, in apparently healthy subjects.

It is conceivable that the occurrence of CEA (a glycoprotein molecule), in non-neoplastic conditions, could be, in part, due to the release of glycoprotein moieties from the various types of cells which have cross-reacting antigenic specificities with known colonic carcinoma CEA. This possibility is strengthened by results of Nery, Bullman and Barsoum described in *Nature New*

Biology next Wednesday (November 14).

Noting that the levels of CEA in the plasma of fresh blood specimens may increase on storage of the whole specimen, Nery *et al.* set about to see if CEA-like cellular components are gradually released into the plasma by red cells. Using isolated red cell membranes they indeed detected CEA by radioimmunoassay; furthermore, red cells from cancerous and non-cancerous patients as well as healthy control donors were positive and all gave similar mean values. Further analysis of the CEA-like substances demonstrated that they have glycoprotein and glycolipid structures, partially cross-react immunologically (as defined by double diffusion in agarose) with known colonic carcinoma CEA, and have molecular weight characteristics similar to colonic carcinoma CEA. The CEA activity was assessed to be probably more than a single structural entity.

It would seem, as Nery *et al.* cogently point out, that what is known as 'immunologically defined CEA' may in fact represent a family of antigenically related molecules, possessing subtle structural differences, perhaps resulting from impaired cellular metabolism. For those who are concerned with assay of CEA, or indeed of any purified tissue antigen, the implications are self-evident.

Mosley (*Can. med. Ass. J.*, **106**, 427; 1972) reported further data which implicated intimate personal contact. During a study of the secondary attack rates of hepatitis among household contacts of patients treated by maintenance haemodialysis the incidence of the infection among children and non-spouse adults was 1.4%, whereas the rate in marital partners was 20%.

Three more recent studies in London tend to substantiate the possibility that sexual transmission of hepatitis B infection may be a real entity. Jeffries and colleagues (*Brit. med. J.*, **2**, 455; 1973) examined serum specimens from 1,650 patients attending a venereal disease clinic in London. Hepatitis B antigen was detected in the serum of 2 out of 553 (0.4%) female patients; 1 out of 520 (0.2%) European male heterosexual patients; and in 11 out of 282 (3.9%) European male homosexuals. The possibility of venereal transmission of hepatitis B infection in homosexuals had been suggested previously. Many of the homosexual patients in this survey attended the clinic repeatedly with genital and skin sores and transmission of hepatitis may have occurred through these lesions.

In another survey conducted by Fulford and colleagues (*Lancet*, **i**, 1470; 1973), sera from 974 patients attending another clinic for sexually transmitted diseases were tested for hepatitis B antigen and antibody. The antigen was detected in the serum of 1.7% of the clinic patients and antibody in 4.8%, whereas in the new blood donor population the overall prevalence was 0.2% and 0.4% respectively (bearing in mind, of course, that these two populations are not strictly comparable). Statistical analysis revealed significant differences for sex and marital status, with both the antigen and antibody-positive groups containing a higher proportion of single men. Highly significant correlations were found for the hepatitis B antibody group with a history of both syphilis and gonorrhoea. Patients with antigen had a significantly higher frequency of gonorrhoea. It was again noted that the group with hepatitis B antibody (which constitutes evidence of past infection with hepatitis B virus) contained a much greater proportion of homosexuals and also promiscuous patients of British origin. In yet another investigation on the mode of spread of acute hepatitis B (Heathcote and Sherlock, *Lancet*, **i**, 1468; 1973) sexual contact or close domestic contact seemed to be the most likely source of infection in 40% of 67 patients studied.

It seems, therefore, that the concept of hepatitis B as an important sexually transmitted infection merits careful consideration not only because it represents a new epidemiological entity but also because prevention may be feasible.

RIBOSOMAL RNA

Control of Synthesis

from a Correspondent

ALTHOUGH the multiple ribosomal RNA genes (rDNA) of *Xenopus laevis* are probably the best characterised of any eukaryotic organism, very little is known about the control of rRNA synthesis. The genes are linked at one locus which is very closely associated with the nucleolus organiser region, since a deletion, which obeys simple Mendelian rules, eliminates both rDNA and nucleolus organiser together. Each gene consists of two parts; the transcription unit which produces ribosomal precursor RNA containing 18, 28S and excess transcribed spacer sequences, and a spacer unit which is not transcribed. Another species of *Xenopus*, *X. mulleri*, also has multiple rRNA genes and a detailed comparison (Brown, Wensink and Jordan, *J. molec. Biol.*, **63**, 57; 1972) between the rDNA of *mulleri* and *laevis* has revealed several interesting things.

Briefly the two sorts of rDNA have different base compositions which is reflected in the slightly greater buoyant density of *laevis* rDNA. Even though it is impossible to distinguish between *laevis* and *mulleri* 18 and 28S rRNA on the basis of size, base composition, or fidelity of nucleic acid hybridisation, the two precursor rRNAs may be distinguished by nucleic acid hybridisation in the presence of excess 18 and 28S rRNA. The species difference is thus due to altered base sequences within the transcribed and non-transcribed spacer regions.

In the latest issue of the *Journal of Molecular Biology* (**80**, 217; 1973) Honjo and Reeder describe the synthesis of rRNA in hybrid frogs produced by crossing *Xenopus laevis* and *mulleri*. Using the notation l^+/l^+ and m^+/m^+ to describe the homozygous wild type ribosomal genotype of *laevis* and *mulleri* respectively and l^-/l^+ to describe the *laevis* heterozygote ribosomal genotype (a similar m^-/m^+ genotype has not been described in *mulleri*), it is possible to write the genotypes of the four possible hybrid animals as follows: l^+/m^+ , m^+/l^+ , l^-/m^+ , and m^+/l^- , given that the maternal contribution is written first.

What Honjo and Reeder have done is to measure the relative transcription of *laevis* and *mulleri* rDNA in these four hybrid types at different stages of development as well as in adult animals. Since it is impossible to distinguish 18 and 28S rRNA from the two species, they had to develop a technique for measuring relative amounts of *laevis* and *mulleri* rRNA based on detection of the non-conserved regions of the precursor rRNA. This was done by hybridisation of a mixture of authentic ^3H -labelled *laevis* precursor rRNA with ^{32}P -labelled precursor rRNA from the

hybrid animal to purified rDNA from both *laevis* and *mulleri* in the presence of excess unlabelled 18 and 28S rRNA. The results are expressed as the ratio (L/M) of $^3\text{H}/^{32}\text{P}$ bound to *laevis* rDNA (L) to $^3\text{H}/^{32}\text{P}$ bound to *mulleri* rDNA (M). They constructed a standard curve of the ratio L/M against the proportion of *mulleri* rRNA in a known mixture of ^{32}P -labelled *mulleri* and *laevis* rRNA and used this for assaying unknown mixtures.

The results of their experiments are briefly as follows: when a hybrid receives *laevis* rDNA (that is, genotypes l^+/m^+ and m^+/l^+), *mulleri* rDNA is repressed; but when a hybrid receives no *laevis* rDNA (that is, genotypes l^-/m^+ and m^+/l^-), *mulleri* rDNA is repressed only if the maternal contribution is *laevis* (l^-/m^+) and then repression is only transitory since by 100 h of development synthesis of *mulleri* rRNA is the same as in the m^+/l^- hybrid which shows no repression of the *mulleri* rDNA.

Honjo and Reeder interpret these results as indicating two pathways for the repression of *mulleri* rDNA. One, due to the presence of *laevis* rDNA, is permanent and not maternally inherited, and the other, due to the presence of *laevis* egg cytoplasm, is maternally inherited and transitory. Clearly these observations may represent two points on the same repression pathway; the cytoplasmic maternally inherited repressor may be identical with the diffusible intermediate operating in repression by *laevis* rDNA, though as they point out the mechanism of repression by *laevis* rDNA may be due to its higher affinity for some molecule in short supply and not to its coding directly for a repressor molecule.

Regardless of the details of the repression mechanism, it seems fair to say that it has something to do with the spacer regions of rDNA since there are apparently no differences between the 18 and 28S rRNA sequences of the two species themselves, and the spacer regions are known to have diverged. This suggestion relies on the assumption that the l^- deletion of rDNA and nucleolar organiser removes no other genetic component which might act as the source of repressor. In this connection it would be interesting to know whether and to what extent the partial nucleolar mutants (Miller and Gurdon, *Nature*, **227**, 1108; 1970; Knowland and Miller, *J. molec. Biol.*, **53**, 321; 1970) of *laevis* will repress *mulleri* rDNA.

Laevis/mulleri hybrids have also previously been used to distinguish between 'chromosome copy' and 'episome' models for rDNA amplification during oogenesis (Brown and Blackler, *J. molec. Biol.*, **63**, 75; 1972). Brown and Blackler found that, regardless of whether *laevis* was the male or female parent, hybrid female animals always amplify

the *laevis* rDNA even though they contain both *laevis* and *mulleri* rDNA complements, which is consistent with the 'chromosome copy' mechanism but not with the 'episome' model since the latter demands maternal inheritance. It is not known at present whether the mechanism for repression of *mulleri* rRNA synthesis has anything to do with the selective amplification of *laevis* rDNA, although the mechanism of rDNA amplification proposed by Crippa and Tocchini-Valentini (*Proc. natn. Acad. Sci. U.S.A.*, **68**, 2769; 1971) based on RNA-dependent DNA synthesis would specifically predict amplification of only *laevis* rDNA if *mulleri* rRNA synthesis is repressed.

WILDLIFE

Death on the Road

from a Correspondent

THE question of what motivates a domestic fowl to traverse a highway has occupied the mind of man ever since roads were invented and chickens were domesticated. This problem was not solved at a symposium entitled "Motorways and the Biologist" which was held at the North East London Polytechnic on October 25, but similar questions were raised; such as the reason why deer and badgers make suicidal excursions across trunk roads and motorways and how they can be discouraged.

D. Venner (Forestry Commission) described attempts to discourage deer from crossing roads in the Forest of Dean by mounting 3-inch square mirrors on posts at the side of the roads which reflect motorcar headlights into surrounding woodland and give animals advance warning of approaching vehicles. The highly predictable nature of deer in both the time and location of crossing roads can be used to advantage in planning the siting of such mirrors. Unfortunately, the data on deer mortality before and after the erection of mirrors are ambiguous and adequately controlled experimentation is needed before this system can be evaluated.

Badgers are also creatures of habit and they often insist on using their well-worn trails between sett and foraging ground even when a motorway is constructed across them. M. Clark and E. P. Ratcliffe described experiences in Hertfordshire and Cheshire respectively in which elaborate attempts have been made to accommodate the inflexible attitudes of local badgers disturbed by motorway construction. In certain situations, where badger trails are well known, special culverts have been incorporated into the design of new motorways, together with badger-proof fencing which channels the animals into the tunnels. Stream culverts can easily

be modified for badger use, but it costs £1,200 to construct a culvert 1 m in diameter especially for badgers. One must admire the motivation behind such expenditure, but so far only circumstantial evidence exists that badgers have demonstrated their appreciation by using these tunnels. It is possible that in the long term a great deal of money could be saved if research into such problems were commissioned before such expenditure was incurred.

The other major topic considered at this meeting was the value of Britain's motorway verges for wildlife conservation. J. M. Way (Nature Conservancy, Monk's Wood) has conducted a survey of the plant life of the M1 motorway between Hendon and Leeds and has found more than 380 plant species on its verges. It is possible to devise management procedures in which the demands of the highway engineer can be reconciled with the desires of the botanist. Some of the most interesting plant communities of verges develop in situations where rocks such as chalk and limestone, which may be exposed by excavation, have not been covered by topsoil after construction. Perhaps arrangements could be made to leave such areas bare. Herbicide treatment is obviously not conducive to a varied flora, nor is it necessarily in the economic interest of those managing a verge. Experiments on cutting frequency reveal that just two mowings, one in May and a second in June, can be effective in maintaining vegetation below 30 inches in height (the recommended level), thus avoiding any herbicide treatment.

The conservation of roadside flora may have some economic as well as amenity value. J. Free (Rothamsted Experimental Station) in a survey of the M1 near St Albans found sixty-seven insect species, of which hoverflies constituted the most important group, carrying pollen on their bodies from a total of thirty-nine plant species. Verges with a high floral diversity may thus act as reservoirs for such beneficial insects.

A further consideration in the conservation of verge flora and fauna is pollution. P. Williamson (Portsmouth Polytechnic) described a survey of lead pollution on the verge of A1 (M) at Catterick. Traffic levels during the survey period were 34,000 vehicles per day. Lead, presumably originating from exhaust fumes, attained levels of 200 p.p.m. in the soil of the central reservation and at the edge of the carriageway. Pitfall traps were used to sample invertebrate populations at various distances from the carriageway and their lead concentrations were measured. Isopoda beside the road were found to contain 700 p.p.m. lead and Diplopoda 100 p.p.m., but despite this the species composition of the invertebrate communities did not seem to be affected by lead. Lead accumulation of this order was not reflected in small mammals, which had liver concentrations of only 10-15 p.p.m. and there was no evidence of further concentration at higher levels in the food chains.

The overall impression given by this conference is that the biologist is not yet in a position to solve many of the ecological problems posed by motorways.

Thiols and Membrane Structure

In the next issue of *Nature New Biology* (November 14) Dupont and Hasselbach describe some extensive changes in the structure of the sarcoplasmic reticulum membrane that ensue when the ATPase is poisoned by thiol reagents. Titration with a mercurial, or with N-ethylmaleimide, reveals that there are ten to twelve reactive thiols per 10^5 molecular weight of protein in sarcoplasmic reticulum vesicles. The two types of ATPase activity that reside in this membrane respond differently to the elimination of free thiols: calcium-activated ATPase decreases linearly while four groups are reacted, whereas the basic magnesium-dependent ATPase evinces slight activation until five of the thiols have reacted, and thereafter falls off rapidly.

That extensive structural changes accompany the reaction of the thiol groups was at once apparent from an increase in turbidity, betokening aggregation of the vesicles. The changes are reflected in progressive alterations in intensity and position of the X-ray

spacings obtained from stacked oriented membranes. These are of relatively minor extent at low levels of substitution, but when more than about four thiols groups have been blocked the character of the X-ray pattern changes in a manner that can be interpreted in terms of the loss of the asymmetric structure which characterises the native membrane. The protein is not released but redistributed so that its average disposition with respect to the plane of the bilayer is symmetrical.

It seems then that substitution of the thiol groups causes the protein molecules to sink into the bilayer, either continuously or, according to a plausible hypothesis offered by the authors, on dissociation of a putative ATPase oligomer, which occurs when a critical number of thiol groups has been blocked. This will expose new protein surfaces and the nature of the interaction with the phospholipids in the bilayer will be changed in such a way as to favour a new and symmetrical structure.

Data Processing

from a Correspondent

ELECTRONIC data processing (EDP) has hitherto been used in very few herbaria, mostly for comparatively small projects, and its scope in the larger herbaria, particularly in Europe where most are located, has been hardly considered. An international meeting at the Royal Botanic Gardens, Kew, from October 3-6, had as its purposes to explore areas where EDP can help in herbaria and associated collections, and to ensure that future developments in the larger European herbaria shall be as far as possible compatible and their results internationally available. The NATO Eco-Sciences Panel acted as sponsor.

After introductions by Professor J. Heslop-Harrison, representing Kew, Professor J. G. Hawkes, chairman of the organising committee of the meeting, and Dr A. Rannestad, representing NATO, the contributions on the first day were chiefly focused on the scope of EDP in herbaria.

J. P. M. Brennan (Kew) described the priorities for EDP in a principal international herbarium, given that staff and finance are limiting factors. R. Ross (British Museum (Natural History)) spoke on the relationship between herbarium records and others, recognising that most important herbaria are associated with ancillary collections or living collections or, in the case of museums, with collections belonging to other disciplines. D. M. Henderson (Royal Botanic Garden, Edinburgh) discussed the problems presented in adapting label data on specimens for EDP purposes. The importance of this aspect is apparent from one of the resolutions passed at the end of this meeting. A. Gomez-Pompa and J. A. Toledo (National University of Mexico) and A. V. Hall (University of Cape Town) described operational schemes in their collections; the Mexican scheme involves a computerised record of the flora of Veracruz.

The general theme of the second day was to consider various EDP systems currently in use to give delegates an opportunity of asking questions and making comparisons. S. G. Shelton (Smithsonian Institution, Washington) described the ambitious and far-reaching Flora North America project—a data bank which uses the GIS system. The general collections at the Smithsonian Institution are recorded by a general-purpose information system called SELGEM, which was described by J. F. Mello. D. J. Rogers (University of Colorado) expounded the well-known TAXIR system devised for taxonomic purposes. The principles of general-purpose filing systems as devised

by the Information Retrieval Group of the Museums Association (IRGMA) were described by J. L. Cutbill (University of Cambridge). This system is basic to the programme for computerising the geological collections at the Sedgwick Museum in Cambridge. S. W. and D. M. Greene (British Antarctic Survey, Birmingham) described the principles behind the computerising of some 30,000 herbarium specimens in the Botanical Section of the British Antarctic Survey. F. H. Perring (Biological Records Centre, Monks Wood) spoke on EDP operations at the centre and made the point that many data can be handled by non-computerised methods, particularly microfilm and microfiche.

Many herbaria are linked with botanic gardens, the computerisation of whose living collections presents, of course, parallel problems. R. A. Brown (American Horticultural Society) described the recording system used at the Plant Records Center where a standardised system has been developed for recording and reporting information on plants cultivated in the principal North American botanical gardens and arboreta. At present the data files contain more than 170,000 records. This theme was later developed by J. Cullen who described the operation of the living plant record system at the Royal Botanic Garden, Edinburgh.

EDP systems in herbaria thus have an interface with similar systems for living collections. With the probable future international development of genetic resource centres, this is likely to increase in importance. Other discussions included the important application of herbarium label data to computerised mapping of plant distributions as developed in the National Herbarium of Canada in Ottawa. A further example was provided by D. B. Williams (British Museum (Natural History)) who discussed the link often found in principal museums between botanical and zoological collections, and described some of the special problems of the latter.

During the conference, recommendations were invited from participants, which were edited by a drafting committee, and put to discussion and vote by the delegates on the last day. The following is a summary of the principal resolutions which were passed, all of them either unanimously or by a very large majority:

(1) Data banks for plant collections should have a common minimal-standard set of descriptors based primarily on label data.

(2) A working party is to be set up to advise European herbaria on the set of descriptors referred to under (1).

(3) Individual herbaria should co-operate with national organisations, and national organisations should be en-

couraged to work through the International Committee on Museums (ICOM) towards widely-acceptable international standards of documentation.

(4) A recommendation will be sent to the Organising Committee of the International Botanical Congress, to be held in Leningrad in 1976, that EDP in taxonomic collections should be discussed and that consideration should be given to setting up a permanent International Commission to coordinate this.

(5) The working party will also consider systems and the possibility of establishing a pilot project in Europe.

(6) The working party will consider and advise on steps to form an international type-register.

(7) Relevant bodies should be encouraged to approach the appropriate United Nations agencies, particularly UNESCO and UNEP, to obtain funds for data banks on a national and international scale.

CELL MEMBRANE

Mobility of Surface Sites

from a Correspondent

MEMBRANE fluidity is certainly one of the most pervasive themes to have emerged in cell biology in recent years. The casual reader will be forgiven for believing that many cell biologists nowadays spend a considerable part of their time moving proteins around a sea of membrane lipid in a delightful molecular version of childhood pursuits. The carbohydrate binding proteins, for example concanavalin A which binds specifically to glucose or mannose-containing structures, are favourite probes for studying the mobility of molecules in the plane of the membrane. It is now widely believed that cell agglutination by con A results somehow from reorganisation of the cell surface to increase the ability of con A receptor sites to move together to form clusters and in the extreme case to 'cap' at one pole of the cell.

Tagging con A molecules with fluorescein allows application of a simple visual technique to the most sophisticated biological problems. A particularly interesting example has been described by Inbar, Ben-Bassat, Fibach and Sachs (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 2577; 1973) who have found that the ability of mouse myeloid leukaemic cells to differentiate into phagocyte cells is related apparently to the fluid state of the surface membrane. Earlier work by Sachs and his colleagues had shown that normal undifferentiated haematopoietic cells transform *in vitro* into mature differentiated macrophages and granulocytes. Devel-

opment of macrophage and granulocyte colonies from single, normal undifferentiated cells requires constant interaction, presumably at the cell surface, with at least one specific mediator. The mediator is a protein with a molecular weight of about 65,000 that requires a small co-factor for activity (replaceable in certain conditions by adenine derivatives including cyclic AMP), and is released by various types of cells in culture into the tissue culture medium. The myeloid leukaemias contain two types of cells, only one of which can be induced to undergo normal differentiation. Again MG1 is needed but the leukaemic cells supply their own, as yet unidentified, co-factor. A clear difference between the two cell types was found by the ability only of the differentiation-competent cells to 'cap' con A molecules bound to their surface. In agreement with older results with normal lymphocytes, normal and virally transformed fibroblasts, clustering or 'cap' formation induced by cross-linking of membrane sites by con A was blocked by metabolic inhibitors, 'freezing' the membrane with aldehyde fixatives or simply by dropping the temperature. Again as often found in such cases, trypsinisation of differentiation-incompetent cells increased the mobility of con A binding sites and caps were formed.

Although thousands of similar observations have been described in a wide variety of systems, the molecular basis for increased mobility of surface sites is still obscure. A direct effect on the viscosity of the membrane lipids seems unlikely. The observation of Inbar *et al.* that 'cap' formation was helped by adding antibodies against con A, or of glycogen, after con A binding suggests that the surface sites were simply too widely spaced to form unaided the necessary cross-linked matrix with the lectin. Edelman *et al.* (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 1442; 1973) suggest that the movement of surface sites is controlled by proteins attached to the inner cytoplasmic face of the surface membrane, the activity or concentration of which is altered. Certainly interaction between these internal proteins and external surface glycoproteins, that may span the cytoplasmic membrane, seems probable.

Whatever the true explanation turns out to be, however, the conclusion of Inbar *et al.* is that a difference in membrane fluidity of specific sites may explain differences in the ability of leukaemic cells to respond to the differentiation-inducing stimulus of MG1. It is now of some interest to correlate more directly the mobility of cellular MG1 receptor sites with the differentiation competence of those cells. Similarly one is curious about the behaviour of normally differentiation-incompetent

cells in an environment containing MG1 and low amounts of trypsin. Whatever the outcome there is no doubt that the experimental substance of this report will appear again and again in discussions of mechanisms controlling other facets of cell development.

INSECT METAMORPHOSIS

Competence to Moul

from our Insect Physiology Correspondent
It has long been known that when the 'imaginal disks' from young larvae of *Drosophila* are transplanted into larval hosts that are ready to pupate, they are unable to differentiate into adult structures. They gradually become competent for imaginal differentiation towards the end of the second instar, 50 to 70 h after hatching. The stimulus for the initiation of metamorphosis is a high concentration of the moulting hormone ecdysone.

In a short but interesting paper Mindek and Nöthiger (*J. Insect Physiol.*, **19**, 1711; 1973) describe a renewed attempt to discover the nature of the changes which result in the acquisition of competence. The experiments consisted in exposing eye-antennal disks removed from donor larvae 53 h old, which are completely incompetent for metamorphosis at this stage, and treating them in various ways before testing their competence by implantation into mature larvae, just before pupation at 120 h. Disks were maintained in adults receiving normal food, in adults 'starved' by feeding on sugar alone, or adults starved for a time and then given normal food. The results show that

competence to respond to ecdysone does not simply require a minimum number of cells (a 'critical mass'); nor is it determined by the time elapsed since the formation of the disk.

The authors conclude that cell divisions are the prerequisite for gaining new developmental possibilities and that a minimum number of cell divisions is needed to allow the necessary changes in the developmental programming of the cells.

PROTEIN SYNTHESIS

Control Mechanisms

from a Correspondent

EXPERIMENTS with mammalian cells in culture have revealed many diverse situations in which the rate of initiation of protein synthesis is greatly reduced. Besides the now classical example of rabbit reticulocytes deprived of haem, inhibition of initiation is seen when cells enter mitosis, are shifted to 42° C, starved of serum or an essential amino acid, infected with poliovirus or exposed to anaerobiosis. In some cases the inhibition is selective; more often the inhibition appears to affect all proteins to the same extent, but, apart from the inhibition of globin synthesis in the absence of haem, very little is known about the underlying control mechanisms. One reason for this is that extracts of cells other than the reticulocyte show almost no initiation on endogenous messenger RNA, so that normal and inhibited cells cannot easily be compared *in vitro*. This impasse has been present for a long time and only

Secondary Structure in an RNA Molecule

As soon as the primary structure of an RNA molecule is elucidated its discoverers set about the happy task of looking for possible secondary structures. When these are published they have tended to elicit alternative secondary structures from competing workers. How can a choice between these alternatives be made? The answer requires a means of assessing the free energy of a given structure and this in turn requires basic information concerning the free energy changes attendant on the formation of the various features—such as base pairs, hairpin loops, interior loops, bulges—which constitute the structure. Each new investigation of the thermodynamics of the secondary structure in oligonucleotides and other simple models leads to a refinement in these calculations.

In their latest paper Tinoco *et al.* (see *Nature New Biology* next Wednesday, November 14) amass recent results for

the sequence dependence of the free energy of formation of base pairs as well as that of various types of bulge and loop. The result is a table of free energy changes from which the total change on forming a given structure from the random coil state at 25° C can be calculated. Each entry in the table, it is claimed, is good to 10% but the uncertainty in the final figure may be somewhat greater; the authors also point out that the algorithm they describe does not take any account of tertiary structure. Nevertheless, it may serve to eliminate some of the more improbable models even if it does not allow a definitive assessment as to which is the most stable.

Tinoco *et al.* suggest that their work may lead to attempts to refine the theory and the experimental data on which it is based and even lead to investigation of temperature dependences which would be highly relevant to the interpretation of melting curves.

now, with a recent paper by Reichman and Penman (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 2678; 1973), does it show any signs of being overcome.

Earlier work by Penman's group had shown that HeLa cells incubated at 42° C recover from the inhibition of initiation after 1–2 h. This recovery is prevented by actinomycin D, but not by cycloheximide, and, in fact, preincubation of cells at 37° C with low doses of this drug makes them less susceptible to inhibition of initiation at 42° C. These and other results suggested that when protein synthesis is slowed down, for example by high temperature, amino acid starvation or cycloheximide, the cells respond by making an RNA which promotes initiation. This RNA was predicted to have a half-life of about 1 h and to be rate-limiting for initiation in certain conditions.

When Reichman and Penman first tested extracts of normal HeLa cells for initiation *in vitro* they, like many others before, found very low activity, as measured by the pactamycin-sensitive incorporation of (³⁵S)-methionine into the N-terminal position of polysomal-bound nascent protein at 25° C. Bearing the earlier results in mind, however, they preincubated their cells for up to 4 h in the presence of a low concentration of cycloheximide and then prepared cell-free extracts, which showed up to six times more initiation. This increase in initiating capacity was prevented by preincubation with cycloheximide and actinomycin D, but was obtained when cells were preincubated in the absence of an essential amino acid. Developing the earlier model, Reichman and Penman suggest that the factor synthesised by intact cells in response to a reduction in protein synthesis is also the factor which is rate limiting for initiation in cell-free extracts, but they are somewhat more cautious in predicting that the factor is an RNA species. Although preliminary, these results open up exciting new possibilities for studying the control of initiation in mammalian cells.

PEAT

Origin of Palsa Mounds

from our Plant Ecology Correspondent

THE energy exchange properties of palsa mounds is the subject of a recent paper by Railton and Sparling (*Can. J. Bot.*, **51**, 1037; 1973), who provide a new approach towards understanding these mounds of peat with frozen cores which are abundant in the mires of high latitudes.

The word 'palsa' originated in Lapland and most of the research which has been undertaken on these features has come from Finland and the Soviet Union. In Finland palsas are only

found north of the coniferous forest limit in areas with a mean annual air temperature of –1° C and an annual precipitation of less than 400 mm. The palsas of that region are often irregularly shaped and may attain lengths of 200 m.

In the search for an explanation of the origin of these phenomena an initial question requiring solution is the start of their formation. By means of pollen analysis accompanied by radiocarbon dating, Salmi (*Proc. 3rd Int. Peat Congr., Quebec*, 182; 1968) came to the conclusion that palsas in Lapland fall into two groups, one of which began formation around 5000 BC and the other at about 3000 BC. The age of a palsa, however, did not seem to be related to its size. Other Finnish workers have found palsas of more recent origin and are less inclined to regard palsas as relics of past climates.

Railton and Sparling align themselves with those who believe in a continuous cycle of formation and erosion of the palsa mounds. They base this belief on their observation that all size classes of palsas are represented in their study area in northern Ontario and also that these classes exhibit a complete intergradation. They do not attempt to justify the assumption that palsa size is a function of palsa age, an assumption which appears rather tenuous in the light of Salmi's work.

They do, however, demonstrate some interesting relationships between palsa size and vegetation cover. Palsas containing a high percentage cover of *Sphagnum fuscum* were mainly less than 60 cm high and less than 7 m long. Lichen-rich communities with, for example, *Cladonia alpestris*, *C. floerkeana*, *C. rangiferina*, were found mainly on mounds greater than 60 cm in height. On the basis of these observations Railton and Sparling suggest that palsas develop continuously, and probably originate as *Sphagnum fuscum* hummocks on the mire surface. They become invaded and dominated by lichens during growth and finally erode and collapse. It is possible that the changes in heat exchange properties associated with the development of a lichen cover could account for the process of palsa development.

To test the feasibility of such a model Railton and Sparling measured the energy exchange properties of the different vegetation types. Total albedo was least on the general mire surface, increased in the *Sphagnum fuscum* hummocks, was greater still in hummocks dominated by lichens and reached a maximum in mature palsas. The obvious question which follows is whether these increases in albedo associated with palsa development are adequate to account for their negative heat budget and hence their growth. A

consideration of the total energy budgets of palsas led Railton and Sparling to the conclusion that the differences in albedo were not sufficiently great when compared with other energy exchange factors, and they are inclined to regard changes in the soil heat flux as being of greater importance. Thermal conductivity in peat decreases as the peat dries. Drier peat on the top of hummocks would lose heat less rapidly in summer, so helping to preserve the permafrost core. If this is so, then the lichen cover so often associated with mature palsas should be regarded as a product of mound development rather than a cause.

PLATE TECTONICS

Subduction Heating

from our Geomagnetism Correspondent

ACCORDING to the hypotheses of the new global tectonics, oceanic trenches, where colder oceanic lithosphere descends into the warmer underlying mantle, should be regions of relatively low surface heat flow; and this prediction is generally confirmed by observation. But observation also shows that behind oceanic trenches (that is, on the side of the trench opposite the spreading ocean floor) the heat flow is above average and associated with the volcanic island arcs. For some years after the basic principles of seafloor spreading and mantle convection had been mapped out, the causes of the volcanism and high heat flow, though clearly related in some way to global tectonic processes, remained obscure, and even today are far from being completely understood. In 1968, however, Oxburgh and Turcotte (*Nature*, **216**, 1041; 1968) and McKenzie and Sclater (*J. geophys. Res.*, **73**, 3173; 1968) made a significant advance by proposing independently that the origin of behind-trench phenomena lies in frictional heating on the slip zone between the descending lithospheric plate and the overlying mantle.

Such frictional heating certainly seems to be able to account for the surface observations behind oceanic trenches; and so several workers have attempted in various ways to calculate the subsurface temperature distribution in the descending plate. Turcotte and Oxburgh (*Phys. Earth planet. Inter.*, **1**, 381; 1968) and McKenzie (*Geophys. J.*, **18**, 1; 1969), for example, assumed in their calculations that the temperature is constant at the slip zone, whereas in later work McKenzie (*Tectonophysics*, **10**, 357; 1970) and Griggs (*The Nature of the Solid Earth*, McGraw-Hill; 1972) assumed the slip zone temperature to be equal to that of an undisturbed mantle. Then again, Oxburgh and Turcotte (*Bull. geol. Soc. Am.*, **81**, 1665; 1970) assumed that the

shear stress on the slip zone decreases with depth, whereas Minner and Toksöz (see, for example, *Tectonophysics*, **10**, 367; 1970) incorporated shear stress heating on both boundaries of the descending slab. But as Turcotte and Schubert (*J. geophys. Res.*, **78**, 5876; 1973) now point out, in these calculations little or no attention has been given to the positions of the volcanic chains behind ocean trenches—that is, to the geometry of the very system resulting from the thermal phenomena under investigation.

With the upsurge in geophysical activity during the past decade or so, many such volcanic chains have become quite familiar; and examples include the Kurile Islands, the West Indies, the Volcano and Mariana islands, Sumatra and Java, the Tonga and Kermadec islands and the New Hebrides. Turcotte and Schubert now propose that all these volcanoes lie above the points on the various slip zones where melting of the descending crust takes place. This assumes, of course, that the magma produced at the slip zone rises vertically to the surface, presumably under the buoyancy force arising from low magma density. Because the hydrostatic pressure is at least an order of magnitude greater than the ultimate strength of the rock at the depths of 100–200 km where the magma forms, the magma will probably move through the rock by the rock's plastic deformation rather than through a fracture; and in the absence of any other preferred direction, this movement will be vertically upwards. Accepting this geometry, the positions of the volcanoes may then be related to a specific process (melting) taking place on the slip zone and thus give an additional fixed point in calculating the subsurface temperature distribution.

Turcotte and Schubert develop two different models of heating on the slip zone. In the first, the shear stress along the slip zone is assumed to be constant down to the depth at which the basalt solidus temperature is reached; and thereafter the temperature at the slip zone remains at the basalt solidus (which increases with depth, of course). In the second model, the shear stress on the slip zone is allowed to increase linearly with depth to the point at which the solidus temperature is reached; and again, temperatures at greater depths are assumed fixed at the basalt solidus. Since the linearly increasing shear stress is equivalent to a constant coefficient of friction on the slip zone, the two models may be characterised, respectively, as 'constant shear stress' and 'constant friction'.

To cut a long physico-mathematical story short, what emerges from the Turcotte-Schubert analysis is an equation for each model which may be com-

pared with observation. In the case of the constant shear stress model, the operative equation gives shear stress in terms of the thermal properties of the system, its geometry (including the vertical distance from the volcanoes to the slip zone) and the velocity of the descending plate. Feeding in observational values for eight individual trenches gives shear stresses in the range 1.18–1.60 kbar, with a mean of 1.35 kbar and a standard deviation of 10%. For the constant friction model, the operative equation is for coefficient of friction in similar terms but with the addition of the mean density above the slip zone. Frictional coefficients calculated from observational parameters lie in the range 0.033–0.077, with a mean of 0.054 and a standard deviation of 24%.

In attempting to decide between the two models, these results are perhaps less clear than might have been hoped. Most of the volcano to slip zone distances lie between 100 and 120 km with errors in locating the slip zone estimated to be $\pm 20\%$. More variable distances would clearly have given a more convincing test for the constancy of either the shear stress or the frictional coefficient. Exceptionally, however, the volcano-slip zone distance for the New Hebrides system is 200 km; and the calculated shear stress at 1.31 kbar is much closer to the mean shear stress than the frictional coefficient of

0.033 is to the mean frictional coefficient. This, together with the smaller scatter of the shear stress values for the eight trench systems, leads Turcotte and Schubert to suggest that the constant shear stress model is probably the better of the two, although they are unwilling to commit themselves to a definite conclusion.

By extending their calculations to depths below the melting zone, Turcotte and Schubert go on to determine the thermal structure of the descending plate consistent with each model, on the assumption that the descending plate is largely olivine and thus that heating due to the olivine-spinel phase transformation, as well as adiabatic heating, is important. Other things being equal, the near-surface heating on the slip zone is somewhat stronger for constant shear stress than for constant friction, although for constant friction melting occurs at a slightly shallower depth. Apart from that, however, the temperature profiles are very similar. Finally, the temperatures on the slip zone are in fairly good agreement with those obtained by Toksöz *et al.* (*J. geophys. Res.*, **76**, 1113; 1971) but the minimum temperatures in the descending plate are about a factor of two lower. Turcotte and Schubert thus agree with others that the plate temperatures obtained by Toksöz *et al.* were probably too high, although the reason for the discrepancy is not clear.

Search for the Superheavies

ONE of the more interesting developments in nuclear physics recently has been the prediction by theorists of the existence of superheavy elements. This island of elements, with atomic numbers in the region of 114, lies significantly beyond the heaviest nuclei (numbers 104 and 105) which have so far been artificially produced and owes its possible existence to the extra binding energy and stability associated with the doubly closed nucleon shells at 114 protons and 184 neutrons.

Prediction of the half lives of these elements is particularly difficult, but some calculations have suggested values as long as 10^9 to 10^{15} years, implying that they might be found in natural materials on Earth. Several searches for superheavy elements in natural ores, minerals and so on have already been carried out and the results from one of the most complete are to be published in next Monday's *Nature Physical Science* (November 12).

The work has been carried out by a large group based on the Oak Ridge National Laboratory in Tennessee. The technique which they use relies on the prediction that superheavy elements are very likely to undergo spontaneous

fission and could emit an average of ten neutrons for each fission event; to be compared with values of less than four for presently known spontaneously fissioning nuclides. The neutron multiplicity counter they use records events in which either three, or more than three, neutrons are detected.

The technique has the advantage that bulky samples can be used and no chemical processing is necessary. Materials investigated range from mineral and ore samples, through flue dust and other samples collected during ore processing, to manganese modules and 60 million-year-old sharks' teeth from a depth of 15,000 foot in the Pacific Ocean and meteorites from Mexico.

In spite of this very wide range of samples no evidence was found for spontaneous fission events accompanied by large numbers of neutrons. It seems then unlikely that superheavy elements will be found naturally on Earth and that physicists will have to await attempts to produce them with the heavy ion accelerators now being planned and under construction. The search for the superheavies will no doubt continue.

LIQUID HELIUM

New Excitation

from our Condensed Matter Correspondent
A NEW type of elementary excitation, christened the ^3He roton, may exist in liquid ^3He - ^4He mixtures according to a calculation by Stephen of Rutgers University and Mittag of the University of Miami, published in a recent issue of *Physical Review Letters* (31, 923; 1973) and based on a suggestion made by L. P. Pitaevski during the United States-Soviet symposium on condensed matter at Berkeley in May.

Below its superfluid transition temperature T_λ , liquid ^4He can be regarded as an inert superfluid background in which exists a gas of elementary excitations carrying all the entropy of the liquid and thus being responsible for its thermodynamic properties. At zero temperature there are no excitations but, as T is increased, the density of the excitations, known as the normal fluid density (ρ_n), increases until at T_λ it is equal to the overall density of the whole liquid. In pure liquid ^4He , except very close to T_λ , there are two distinct types of elementary excitation: at small momenta, the energy ϵ of an excitation is directly proportional to its momentum p , and it is thus a phonon, or quantum of sound; at higher momenta there is a minimum in the $\epsilon(p)$ curve, and the excitations, all of energy close to Δ , existing in this region are known as rotons. Their physical nature is not entirely clear, but they may, perhaps, be the microscopic quantum mechanical analogue of classical vortex rings.

The addition of small proportions of ^3He profoundly affects the properties of the liquid. The ^4He atoms act as additional excitations, and thus increase the normal fluid density and contribute to the thermodynamic properties. Measurements of the heat capacity and wave velocity at very low temperatures have shown that a ^3He atom behaves very much like a free particle in that its energy varies as the square of its momentum, but with a modified mass m_3^* to take account of the superfluid background through which it moves.

When Sobolev and Esel'son made direct experimental measurements of ρ_n (*Zh. éksp. teor. Fiz.*, 60, 240; 1971) they found that ρ_n seemed to increase with ^3He concentration much more rapidly than expected. Since the contribution to ρ_n from the ^3He atoms is just $n_3 m_3^*$ where n_3 is their number density, and that from phonons at any given temperature depends only on the velocity of sound which does not change much with n_3 , it was concluded that the effect must be associated with a decrease in the roton energy Δ . Recent experimental measurements of Δ by Surko and Slusher of Bell Laboratories, and independently by Woerner, Rock-

well and Greytak of MIT, both using light scattering techniques and reported in the same issue of *Physical Review Letters* (30, 1111 and 1114; 1973) have shown, however, that Δ does not change significantly with ^3He concentration.

It was this apparent contradiction in the experimental evidence for the value of Δ which led Pitaevski to suggest that the $\epsilon(p)$ curve for ^3He excitations in liquid ^4He might also display a minimum, much like the roton minimum. If the value of ϵ at the minimum were less than Δ , then there would clearly be a possibility of resolving the conflict.

Stephen and Mittag have now carried out a detailed calculation, using the same theoretical approach as in the original Feynman-Cohen derivation of the $\epsilon(p)$ spectrum for pure ^4He . As Pitaevski had surmised, they find that the ^3He excitation spectrum does indeed display a minimum, that this occurs at an energy lower than Δ , and that it is thus possible to reconcile quantitatively, within-experimental error, the measured values of ρ_n with those of Δ . The probable reason that ^3He excitations near the minimum, referred to as ^3He rotons, were not also observed in the light scattering experiments is, the authors suggest, that the relative intensity of the scattering associated with rotons and ^3He rotons is proportional to the square of the ratio of the ^4He and ^3He number densities, so that, because the proportion of ^3He was always less than 30%, the former scattering process would have been strongly dominant.

Convincing confirmation that ^3He rotons really do exist, however, must probably await the results of further light scattering experiments.

CRYSTAL GROWTH

Crystallite Coalescence

from our Materials Science Correspondent
MASSON and his colleagues in Marseilles have published a series of beautifully executed electron microscope studies of the early stages of condensation of metallic films on ionic substrates; the strikingly novel finding from this work was that small crystallites can wander about in a two-dimensional walk, and, above a certain temperature, the migrating crystallites will coalesce when they touch by chance in the course of their wanderings. These findings have been summarised before (*Nature phys. Sci.*, 241, 1; 1973).

Now some theoretical implications of the Marseilles findings have been worked out by Robertson (*J. appl. Phys.*, 44, 3924; 1973) in a stimulating paper. He starts from the observation (by the Marseilles team and others) that whereas crystallites do in fact coalesce at elevated temperatures (for example, above

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150° C in KCl), they do not at lower temperatures, although other evidence indicates that they do migrate at these lower temperatures. Robertson analyses the predicted coalescence kinetics in terms of migration rates and collision probabilities (which themselves depend on crystallite sizes). It turns out that there should be extensive coalescence under conditions when in fact none is experimentally observed.

Robertson speculates on possible reasons why collisions should not result in coalescence. Three ideas are put forward: the crystallites may in various ways pick up electrostatic charges or the substrate surface may be contaminated; either form of disturbance is known to inhibit coalescence of colloids suspended in fluids. The third source of disturbance, examined in more detail, is the buildup of misfit stresses between substrate and crystallites, and Robertson indicates that the possibly sharp dependence of misfit stress on crystallite size could lead to either enhancement or hindrance of coalescence. He concludes by claiming that the very process of crystallite migration is not yet established beyond all doubt, and that this is a research topic deserving of much more attention, since it may force a complete revision of the classical concept of heterogeneous nucleation and growth.

Irreversibility as a Symmetry-breaking Process

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This article is based on the 1972 Bourke lectures of the Faraday Division of the Chemical Society.

It is just one hundred years ago that Boltzmann published his celebrated paper "Further Studies on Thermal Equilibrium between Gas Molecules"¹, in which he formulated his kinetic equation for the velocity distribution $f(\mathbf{v}, t)$ of dilute gases²

$$\partial f / \partial t = \int d\Omega \int d\mathbf{v} \sigma(\Omega) |\mathbf{v}_1 - \mathbf{v}| (f_1' f' - f f_1) \quad (1)$$

He then introduced the quantity $\mathcal{H}_B$ defined through

$$\mathcal{H}_B = \int d\mathbf{v} f \log f \quad (2)$$

and established as a consequence of equation (1) the inequality

$$d\mathcal{H}_B/dt \leq 0 \quad (3)$$

This basic inequality led him to the first microscopic model of entropy

$$S = -k\mathcal{H}_B \quad (4)$$

Boltzmann used physical intuitive arguments to obtain equation (1). He emphasized that the Second Law of Thermodynamics deals with large systems and that he therefore felt justified in adding to the laws of dynamics additional elements based on probability calculus.

Why are Boltzmann's investigations so central? They link together various levels of description of the physical world which had been introduced independently: classical or quantum dynamics, stochastic theory and thermodynamics.

Boltzmann's $\mathcal{H}$ theorem has led to a strange situation, perhaps unique in the history of science. On one side Boltzmann's kinetic equation has been applied successfully to many physical phenomena such as the calculation of transport properties of gases². More important still is the fact that computations based on molecular dynamics have entirely validated Boltzmann's predictions³⁻⁵. Such computer experiments show that indeed Boltzmann's quantity $\mathcal{H}_B$ decreases with time. (Because of the finite size of the sample, fluctuations appear but they decrease when the size of the sample is increased.)

These numerical experiments are very important, for they show that using only the laws of classical dynamics inequality (3) is satisfied for sufficiently large assemblies of interacting particles. In other words, the effects described by Boltzmann's kinetic equation (1) are in agreement with the results of numerical integrations based on classical dynamics. This gives one a strong incentive to investigate the conditions in which a dynamic system may present "dissipative" properties such as described by inequality (3), without introducing additional non-mechanical elements. I shall show that it is now possible to present a rigorous "mechanical theory" of irreversibility. Here I shall present only a very concise account of some of the chief ideas, omitting all proofs. More information can be found in refs 6, 7 and 8.

Time Reversal Symmetry

I shall start from classical or quantum dynamics as expressed by Hamilton's equations of motion

$$dq/dt = \partial H / \partial p \quad dp/dt = -\partial H / \partial q \quad (5)$$

or Schrödinger's equation

$$i\partial\psi/\partial t = H\psi \quad (6)$$

Both descriptions may be unified through the Liouville-von

Neumann equation for the distribution function (or the density matrix⁹)

$$i\partial\rho/\partial t = L\rho \quad (7)$$

with

$$L\rho = -i\{H, \rho\} \text{ Poisson bracket} \\ [H, \rho]_- \text{ commutator} \quad (8)$$

In both cases L is a hermitian operator (better called a super-operator because it acts on matrices in the quantum mechanical case, see refs 7 and 8). Therefore

$$L = L^\dagger \quad (9)$$

A basic feature of equation (7) is its " Lt invariance". Indeed, under the combined effect of the two operations

$$\begin{cases} L \rightarrow -L \\ t \rightarrow -t \end{cases} \quad (10)$$

equation (7) remains invariant. Note that if L is a possible Liouville operator so is $-L$. The " Lt invariance" expresses in a concise fashion the time reversal symmetry.

Now in spite of the " Lt invariance" some types of irreversible processes are still possible. For the example of a single particle enclosed in a large box the Hamiltonian is

$$H = p^2/2m \quad (11)$$

and equation (7) becomes

$$\partial\rho/\partial t + (\mathbf{p}/m) \cdot \partial\rho/\partial\mathbf{r} = 0 \quad (12)$$

In rather general conditions the density in coordinate space obtained from ρ through integration over the velocities, will become uniform in the box both for $t \rightarrow +\infty$ and for $t \rightarrow -\infty$ (see ref. 9, chapter 8). This is because the spectrum of the operator is continuous (see refs 9-12). Indeed, as can be easily verified (ref. 9, chapter 1) its eigenvalues are

$$\lambda = \mathbf{k} \cdot (\mathbf{1}/m)\mathbf{p} \quad (13)$$

where $\mathbf{k}$ is a real vector the value of which is determined by the boundary conditions.

Less trivial examples have also been considered. For example, one may study chains of harmonic oscillators and follow how equilibrium between kinetic and potential energy is achieved in the limit of large lattices¹³⁻¹⁸. In none of these cases, however, do quantities such as Boltzmann's collision operator or thermodynamic transport coefficients appear. This obviously requires stronger conditions than the continuous L spectrum. This conclusion may already be inferred from the structure of phenomenological equations such as the Fourier equation

$$\partial T / \partial t = \kappa \partial^2 T / \partial x^2 \quad (14)$$

As the heat conductivity κ is a positive quantity its sign cannot be reversed. Therefore the time inversion $t \rightarrow -t$ leads to the different equation

$$\partial T / \partial t = -\kappa \partial^2 T / \partial x^2 \quad (15)$$

This makes a pair of equations in each of which the direction of time plays a different role (in equation (14) the temperature becomes uniform for $t \rightarrow +\infty$, in equation (15) it was uniform for $t \rightarrow -\infty$); by contrast the single equation (12) predicts uniformity for distribution in coordinate space for both $t \rightarrow -\infty$ and $t \rightarrow +\infty$. The time reversal symmetry present in the dynamical description of equation (7) has been broken in equations (14) and (15).

One may say that the Second Law of Thermodynamics

$$dS/dt \geq 0 \quad (16)$$

summarizes in a single inequality all laws such as Fourier's law, friction phenomena and so on which are described by phenomenological equations involving a privileged direction of

time. This is the situation we associate with "thermodynamic irreversibility" and it is with this type of irreversibility that I am concerned here.

To return to the central problem: What are the conditions that have to be imposed on dynamics to obtain this behaviour? I believe that we can now give a precise answer to this question and show that the symmetry breaking is due to the possibility of analytical continuation for well defined dynamic quantities.

Dynamics and Dissipation

I shall first write the formal solution of the parabolic equation (7) in terms of the resolvent of the operator L (see ref. 9).

$$\rho(t) = \exp(-iLt)\rho(0) = (2\pi i)^{-1} \int dz \exp(-izt)(1/L - z)\rho(0) \quad (17)$$

The importance of this formal representation of $\rho(t)$ in terms of the resolvent comes from the fact that this representation incorporates causality (see refs 19 and 20). Indeed the contour c is a parallel to the real axis but has to be taken above or below it according to whether "retarded" solutions for $t \geq 0$ or "advanced" solutions for $t \leq 0$ are considered. The solution $\rho(t)$ is determined both by the differential equation (7) and the choice of the contour.

The formalism which I shall introduce now permits a discussion of the behaviour of the resolvent in the complex plane. The first step is to define orthogonal hermitian projection operators P, Q such that

$$P + Q = 1 \quad (18)$$

The choice of these operators fixes the "language" in which the results are formulated. I shall consider specific examples later. Generally P is chosen to project onto the diagonal elements in the representation in which some model Hamiltonian H_0 is diagonal (using here quantum mechanical notations)

$$\langle m | P \rho | n \rangle = \langle m | \rho | m \rangle \delta_{m,n} \quad (19)$$

As diagonal elements give no information about correlations between particles $P\rho$ is called the "vacuum of correlations".

Using P and Q it is easy to verify the following identity for the resolvent²¹⁻²³

$$\frac{1}{L - z} = \{P + \mathcal{G}(z)\} \frac{1}{PLP + \Psi(z) - z} \{P + \mathcal{D}(z)\} - \mathcal{D}(z) \quad (20)$$

with

$$\Psi(z) = -PLQ \frac{1}{QLQ - z} QLP \quad (21)$$

$$\mathcal{D}(z) = -PLQ \frac{1}{QLQ - z} \quad (22)$$

$$\mathcal{G}(z) = -\frac{1}{QLQ - z} QLP \quad (23)$$

$$\mathcal{D}(z) = -\frac{1}{QLQ - z} \quad (24)$$

These are the basic operators in the formulation of non-equilibrium statistical mechanics. Of special importance is the collision operator $\Psi(z)$: reading equation (21) from right to left it corresponds to a transition from the vacuum of correlations followed by a dynamical evolution in the correlation space and finally followed by a return to the vacuum of correlations. The operator $\mathcal{D}(z)$ corresponds to a transition $P \leftarrow Q$ and is therefore called the destruction (of correlations) operator, similarly $\mathcal{G}(z)$ is the creation (of correlations) operator. All these operators depend both on the dynamics of the system (through the Liouville operator L) and on the language used (through the projection operators P and Q).

The important point is that through the introduction of these operators one can study the limit for $z \rightarrow +i\epsilon$ and the analytic continuation of the resolvent (20).

Insertion of equation (20) into equation (17) leads to an integrodifferential equation for the retarded solution. This equation is generally called the "master equation"⁹ (for recent

applications see refs 24 and 25). Neglecting non-local and memory effects the master equation takes the simple form for the diagonal elements of the density matrix^{8,9}

$$i\partial\rho_0/\partial t = \Psi(0)\rho_0 \quad (25)$$

with

$$\Psi(0) = \lim_{z \rightarrow +i\epsilon} -PLQ \frac{1}{QLQ - z} QLP \quad (26)$$

(P has been chosen in such a way that PLP vanishes.) The collision operator has a specially simple physical meaning in the case of potential scattering. The matrix elements (in momentum representation) $\langle p | \Psi(0) | p' \rangle$ give then directly the scattering cross section for the transition $p \leftarrow p'$ (ref. 26).

In the limit of large systems, the sum over the intermediate states Q (the "correlations") involves an integration. Therefore a formal representation of equation (26) is given by²⁷

$$-i\Psi(0) = -\pi PLQ \delta(QLQ) QLP + iPLQ \frac{1}{QLQ} QLP \quad (27)$$

where the second term is understood as a principal part. If this formal expression is meaningful and each of the two terms exists, it follows that

(a) $-i\Psi(0)$ is split into an even and an odd part with respect to L inversion

$$\Psi(0) = \dot{\Psi}(0) + \ddot{\Psi}(0) \quad (28)$$

(b) the even part is a negative operator

$$-\dot{\Psi}(0) \leq 0 \quad (29)$$

(c) the even part $\dot{\Psi}(0)$ is hermitian while the odd part is anti-hermitian.

All these three properties are quite important. They solve in fact the three fundamental problems which have always faced non equilibrium statistical mechanics. First of all if the even part $\dot{\Psi}(0)$ exists, the master equation (25) obviously loses the Lt invariance. After Lt inversion one obtains

$$i\partial\rho_0/\partial t = [-\dot{\Psi}(0) + \ddot{\Psi}(0)]\rho_0 \quad (30)$$

This is precisely what would have resulted if in equation (17) the contour below the real axis had been taken and the "advanced" solutions constructed. The situation is quite similar to that discussed in the context of the Fourier equation (see equations (14) and (15)).

In the second place inequality (29) shows that the even part may be considered as expressing a "damping" which occurs in the future in equation (25) and in the past in equation (30) (for more details see ref. 6). Therefore inequality (29) contains in a nutshell the Second Law of Thermodynamics, equation (16). More precisely because of equation (29) a microscopic model of entropy can be constructed such that this entropy can only increase (or remain constant) for all initial value problem (see ref. 8 and I. P. and F. Henin, to be published). I shall come back to this question later.

Finally the third property (hermiticity of $\dot{\Psi}(0)$) permits it to be given, at least in simple cases, an interpretation in terms of transition probabilities in the sense of a Markoff chain^{8,28}. It is this property which leads from the initial dynamic description to a description in terms of stochastic processes.

One can see how deeply dynamics is altered when the collision operator $\Psi(0)$ does not vanish. The appearance of an even part in $\Psi(0)$ leads to a radical change in the dynamic description of the system. It should be noted that the discussion has been based on equation (25) rather than the general master equation. A general discussion will be presented later.

Dynamic Systems with Broken Symmetry

The basic importance of the even part $\dot{\Psi}(0)$ leads me to introduce the following classification: (a) $\dot{\Psi}(0)$ vanishes; this

is the situation for quantum systems with a discrete non-degenerate spectrum (then $z=0$ in equation (26) does not belong to the spectrum of QLQ); (b) $\Psi(z)$ becomes undefined when the limiting process $z \rightarrow +i\epsilon$ is performed. This may be the case for quantum system with discrete but degenerate spectrum (for examples see refs 29 and 30). This situation also occurs in classical dynamics when gravitational forces are involved^{31,32}; (c) finally, there is the situation in which $-i\Psi(0)$ is well defined and negative

$$-i\Psi(0) \leq 0 \quad (31)$$

This is the dynamic dissipativity condition. (This terminology agrees with the common mathematical terminology³³.) When satisfied it implies a qualitative change in the structure of the invariants of the system and it is a necessary condition for a thermodynamic type of behaviour. As already noted, inequality (31) cannot occur unless the spectrum of L is continuous. At least for quantum systems this is only possible in the limit of an infinite volume and eventually also of an infinite number of particles (the so-called thermodynamic limit).

For scattering these three cases correspond, respectively, to the situations where the S matrix is unity (no scattering), where the scattering cross section diverges and finally to the situation where the cross section is different from zero, when it is necessarily positive. The dissipativity condition also applies, however, to much more general situations. Examples of N body dissipative systems have long been known⁹. The operator $\Psi(0)$ has been calculated explicitly for systems such as weakly coupled gases or slightly anharmonic solids. In all these cases it is easy to verify that in accordance with our general statement $-i\Psi(0)$ has an even part, is negative and hermitian. For such systems the dissipativity condition has a very simple meaning—that there are processes which conserve energy and momentum such that the integral involved in $\Psi(0)$ (see equation (17) and remarks earlier in this article) does not vanish. This was discussed in detail some years ago (see ref. 9, chapter 14). This interpretation applies, however, only to very simple situations.

The construction of $i\Psi(0)$ may be extended to strongly coupled system using formal perturbation techniques⁸. It is also very instructive to study simple models where a rigorous, non-perturbative approach is possible.

A simple example is given by the Hamiltonian

$$H = \sum_{m,n=-N}^N |m\rangle H_{m,n} \langle n| \quad (32)$$

where $H_{m,n}$ is a hermitian, Toeplitz form characterized by the properties

$$H_{m,n}^N = H_{m-n}^N \quad (33)$$

These systems have recently been studied carefully by Gibberd and Stey, Stey^{29,30} and Grecos³⁴. In the limit $N \rightarrow \infty$ they satisfy rigorously the dissipativity condition (31).

A second example is Friedrichs's model^{28,35-39}. The Hamiltonian is then of the form

$$H = H_0 + \lambda V \quad (34)$$

where H_0 has a continuous spectrum and an embedded discrete eigenvalue ω_0 coupled through the λV perturbation.

The Friedrichs model is related to various models investigated in the literature such as the Wigner-Weisskopf model for a two-level atom, the Lee model in field theory and so on.

As in the case of the Toeplitz forms, the Friedrichs model is soluble, as the transformation which diagonalizes H can be obtained. Because of the continuous nature of the spectrum, H will admit in general both eigenfunctions and eigendistributions (containing δ functions as well as principal parts).

We may choose³⁶ P so that $P\rho$ is the probability of finding the unstable (discrete) state excited at time t . Here again the resolvent of the von Neumann operator as well as $\Psi(z)$ can be obtained by a direct calculation using equations (20) and

(21). It turns out that

$$\Psi(0) = \dot{\Psi}(0) = \left[-\frac{1}{2i\pi} \int_{-\infty}^{+\infty} dx \eta^+(x) \eta^-(x) \right]^{-1} \quad (35)$$

Here $\eta^\pm$ are the limiting values on the real axis of the analytic function

$$\eta(z) = \omega_0 - z - \lambda^2 \int_0^\infty d\omega |\nu(\omega)|^2 / (\omega - z) \quad (36)$$

I assume that the continuous spectrum of H_0 and thus of H extends over the positive real axis; $\nu(\omega)$ measures the coupling between ω_0 and the continuous spectrum.

Because in this case P is a one-dimensional projection, $\Psi(0)$ as given by equation (35) is a number (while in the Toeplitz case Ψ is an operator represented by a matrix).

Using equation (36) we have shown³⁶ that $\dot{\Psi}$ does not vanish if the coupling parameter λ is smaller than a critical value, a condition which implies that H has no point spectrum corresponding to a bound state; $i\Psi$ is essentially the inverse of the life time of the unstable state. These examples establish rigorously the existence of dynamic systems with broken Lt symmetry.

Invariants of Motion and Dissipation

One has to expect a close connexion between the non-vanishing of the collision operator $\Psi(0)$ and the problem of the invariants of motion.

I shall consider a Hamiltonian H together with the projection operator P (see equation (18)) and write

$$H = PH + QH = H_0 + \lambda V \quad (37)$$

This relation defines the "unperturbed" Hamiltonian H_0 . Now suppose that the problem of invariants for PH has been solved; every observable $P\Phi$ commutes with PH and is an invariant of motion. The basic problem will be to study the possible relation between the invariants of H and of PH . Now suppose that Φ is an invariant for the dynamical system. Then

$$L\Phi = 0 \quad (38)$$

The invariants Φ may be classified into regular or singular^{36,37,40}. (Briefly, singular invariants are such that their off-diagonal part $Q\Phi$ does not satisfy the regularity conditions necessary to include it in a Cauchy integral). If both the collision operator $\Psi(z)$ and the creation operator $\mathcal{C}(z)$ (see equation (23)) exist in the limit $z \rightarrow +i\epsilon$, then starting from equation (38) a few manipulations show that regular invariants satisfy the conditions^{36,40,42}

$$\Psi(0)P\Phi = 0 \quad (39)$$

$$Q\Phi = \mathcal{C}(0)P\Phi \quad (40)$$

showing the essential importance of the collision operator. If it were to vanish the result would simply be

$$Q\Phi = \mathcal{C}(0)P\Phi \quad (41)$$

To each invariant Φ_0 of PH , then, corresponds the invariant Φ_0 , $\mathcal{C}(0)\Phi_0$ of H . If, however, $\Psi(0)$ does not vanish then the conditions for regular invariants (39) and (40) are much more restrictive as $P\Phi$ has then to be an eigenfunction of the collision operator corresponding to a zero eigenvalue. Obviously this destroys the one-to-one correspondence between the invariants of PH and the regular invariants of H .

For example, in the Friedrichs model, H has lost the discrete eigenvalue of PH in the dissipative case. The complete set of invariants of H has been calculated and it has been verified that in the dissipative case there exists no regular invariant^{36,40}.

Although dissipativity implies the breaking of the one-to-one correspondence between the invariants of PH and of H , the inverse is not true. Poincaré's work^{9,43} provides simple examples of finite classical systems in which H admits no trivial invariants which are analytical in the coupling constant.

Nonetheless it is easy to show that in these cases the limit (26) does not exist because of the finiteness of the system. The breaking of the correspondence between the invariants of PH and of H is therefore a necessary but not a sufficient condition for dissipativity.

Causal Dynamics

The chief conclusion of my approach here is that dissipative properties correspond to a breaking of the Lt symmetry. This symmetry breaking was, however, obtained through the study of the integral representation (17) which as we have mentioned, includes causality. I shall now establish a differential equation of motion which exhibits explicitly this symmetry breaking and would therefore be the natural generalization of equation (25) valid only for simple situations (such as corresponding to weakly coupled systems). This can indeed be done in terms of a new extended formulation of transformation theory (see refs 8, 28 and 38) and, especially, ref. 44.

To summarize the basic ideas: we may ask what is the relation between the original Liouville equation (7) or its integral representation (17) and an equation such as (25) which contains both odd and even terms. The point of view as developed by our group is that both equations are exact representations of the dynamic evolution of the system. This equivalence should therefore be expressible in terms of a transformation theory which would lead from equation (7) to a new equation

$$i\partial\rho/\partial t = \Phi\rho \quad (42)$$

where the evolution operator Φ would, for dissipative systems, also contain an even part in respect of L .

In other words, one has to consider a relation of the form

$$\rho = \Lambda(L)\rho \quad (43)$$

where the transformation operator Λ depends on L . Indeed substitution of equation (43) into equation (7) yields

$$\Phi = \Lambda^{-1}L\Lambda \quad (44)$$

As both representations (7) and (42) are considered equivalent the transformation Λ should preserve average values of observables, that is, it must be such that

$$\langle O \rangle_t = \text{tr} O^+ \rho(t) = \text{tr} O^+ \rho \quad (45)$$

with

$$O = \Lambda(-L)O \quad (46)$$

$\Lambda(-L)$ has to be used in equation (46) because the evolution operator for observables is, in the Heisenberg scheme $-L$ (and not $+L$ as in the Liouville equation). Moreover the transformation has to preserve the hermitian character of the observables and the density matrix.

An important feature of these transformations is that they are non-unitary but satisfy the condition

$$\Lambda^{-1}(L) = \Lambda^+(-L) \quad (47)$$

It is only for transformations independent of L (or even in L) that one comes back to unitary transformations, but then Φ in equation (44) could not contain both even and odd terms in L . This new class of transformations has been called "starunitary" transforms. It is easily shown that equation (47) leads to the invariance of average values as expressed in equation (45). The generator of time displacement Φ can be viewed as an extension of the collision operator $\Psi(0)$ introduced earlier.

The three basic properties of $\Psi(0)$ discussed earlier are shared by the operator Φ (refs 8, 38 and 45). We may again split Φ into an odd and an even part in respect to L inversion. Equation (42) is valid for the retarded solution. The advanced solution would satisfy an equation similar to (30) in which the sign of the even part Φ is reversed. Therefore causality is explicitly included in this formulation of dynamics. For this reason we have called equation (42) the "causal" formulation of dynamics.

As $-i\Phi$ is a seminegative operator the evolution of dissipative systems may be described in terms of a Liapounoff function. I shall indeed consider the quadratic functional in the causal representation (dropping the superscript ϕ)

$$\Omega = \text{tr } \rho^+ \rho \quad (48)$$

It is easy to show using equation (42) that

$$1/2 \, d\Omega/dt = -\text{tr } \rho^+ (i\Phi) \rho \leq 0 \quad (49)$$

The property (49) implies that the statistical equilibrium corresponding to a minimum of Ω has a very simple meaning in the causal formulation of dynamics: all quantum states have the same probability and random phases.

We may now introduce the quantity $\mathcal{H}$ defined through

$$\mathcal{H} - \mathcal{H}_{\text{eq}} = 1/2 \log (\text{tr } \rho^+ \rho / (\text{tr } \rho^+ \rho)_{\text{eq}}) \quad (50)$$

This corresponds then to a microscopic model of entropy given by

$$S = -k\mathcal{H} \quad (51)$$

Notice that

$$\begin{aligned} \mathcal{H} - \mathcal{H}_{\text{eq}} &\geq 0 \\ d\mathcal{H}/dt &\leq 0 \end{aligned} \quad (52)$$

$\mathcal{H}$ is an additive function for independent systems.

I cannot enter here into a detailed discussion of our quantity $\mathcal{H}$ (50) which gives, in my opinion, the general dynamic interpretation of the Second Law of Thermodynamics (16) (see I. P. and F. Henin, to be published). Briefly, however, the quantity $\mathcal{H}$ (50) corresponds to the approach of the system to microcanonical equilibrium. It can only decrease in time whatever the initial conditions (at least when some regularity conditions are satisfied³⁶). This is a basic difference with Boltzmann's definition (2) which even for dilute gases requires initial conditions compatible with the validity of the kinetic equation (1).

Irreversibility is a dynamic property based on the possibility to subdivide the solutions of the equation of motion into two semigroups corresponding respectively to retarded and advanced solutions. Entropy increases with time for each retarded solution.

Note that because the entropy is a non-linear functional of the density matrix it cannot in general be expressed in terms of observables such as temperature and density. This is only possible in the neighbourhood of equilibrium (ref. 46 and I. P. and F. Henin, to be published). It is only then that both entropy and entropy production acquire a macroscopic meaning. Briefly, the Second Law of Thermodynamics becomes a theorem in dynamics which only near equilibrium can be expressed in terms of macroscopic variables.

I shall finally compare the causal representation to the representation in which the Hamiltonian is diagonal. In such a representation one would have non-interacting excitations. Now obviously in the interaction of systems with continuous spectrum two quite different effects have to be taken into account: a modification of the interacting units ("renormalization") and an overall effect of a thermodynamic nature which expresses that the interaction permits to the system to approach equilibrium. This thermodynamic aspect of interaction has already been emphasized in the classical Einstein work on the interaction of matter with radiation⁷. The star unitarity transformation permits to treat both effects of the interaction. For non-dissipative systems one returns to the usual unitary transformation in which the only effect of the interaction terms is to redefine the excitations.

These problems will be treated more completely elsewhere (see I. P., C. George, A. Grecos and F. Henin, to be published).

Dissipative Structures

I shall now make some remarks pertaining to macroscopic thermodynamics. Once an entropy can be associated with the dynamic evolution of a system it is possible to distinguish between near and far from equilibrium situations.

This leads precisely to a distinction between "equilibrium structures"⁴⁸ which may be understood in terms of classical equilibrium thermodynamics and "dissipative structures". The latter are formed and maintained through the exchange of energy and matter in non-equilibrium conditions. Many examples of dissipative structures in fluid dynamics or non-linear chemical networks are now known. Their formation always requires a minimum distance from thermodynamic equilibrium and their appearance expresses the fact that the "thermodynamic branch", which corresponds to the extrapolation of equilibrium to non-equilibrium situations, becomes unstable against fluctuations.

Of special interest are symmetry-breaking dissipative structures in which the system has the "choice" between various possibilities. The type of initial fluctuations determines the specific dissipative structures which will be realized. Once realized this dissipative structure is stable against the type of fluctuations considered. Successions of instabilities of this type may occur, involving a kind of primitive memory or, so to say, a "historical dimension"^{48,49}. The present structure of the system can only be understood in terms of the succession of instabilities through which it originated.

There seems to be little doubt that there is a close connexion between dissipative structures and biological organization. For example, important biological multi-enzymatic processes have been shown to work beyond the stability limit of the thermodynamic branch. More details may be found in ref. 49. These considerations have to be borne in mind when the problem of the origin of irreversibility is discussed.

I shall conclude this article with some epistemological considerations about the origin of irreversibility. (For more details see refs 50-52.)

The Second Law of Thermodynamics has been repeatedly considered as the basis for the introduction of the concept of irreversibility. Others, on the other hand, base their explanations of irreversibility on biological functions such as memory. My approach leads to a model which incorporates both ideas.

To obtain the dissipativity condition (31) it was necessary to start with the formal solution (17) which as already emphasized, includes causality. Once condition (31) is satisfied, all retarded solutions lead to an increase of entropy in time. Now the incorporation of causality means that the future can at the outset be distinguished from the past. Then, using the laws of mechanics and, specifically, the dissipativity condition, one derives for such systems the existence of a thermodynamic description. In the framework of this description the concept of dissipative structures with their possible time anisotropy may be defined as in the previous section. This sequence may be expressed graphically⁵⁰⁻⁵² as in Fig. 1. Without the distinction between future and past, entropy could not be introduced, but without entropy dissipative structures in which the distinction between past and future is, so to speak, built in, could not be obtained. If we wish we may consider ourselves as a specific dissipative structure. This interpretation of irreversibility means then that we recognize in the outside world classes of objects which have precisely the property (anisotropy of time) which we have attributed to ourselves at the start.

The concept of irreversibility, and especially the Second Law of Thermodynamics, plays an important role in many parts of theoretical physics. Our unified formulation of

dynamics and thermodynamics is therefore likely to open new perspectives for theoretical research.

This article summarizes some aspects of work done by our groups in Brussels and Austin. I thank my colleagues and friends M. de Haan, Cl. George, A. Grecos, F. Henin, F. Mayné, G. Nicolis, L. Rosenfeld and G. Stey for elaboration of the ideas summarized here. This work has been supported by the Welch Foundation, Houston, and the Fonds de la Recherche Fondamentale Collective, Belgium.

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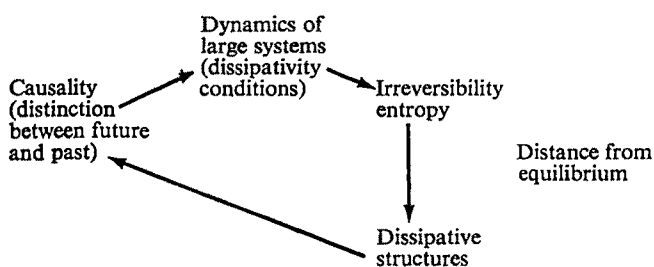


Fig. 1

Eclipse Flight of Concorde 001

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On June 30, 1973, Concorde 001 intercepted the path of a solar eclipse over North Africa. Flying at Mach 2.05 the aircraft provided seven observers from France, Britain and the United States with 74 min of totality bounded by extended second (7 min) and third (12 min) contacts. The former permitted searches for time variations of much longer period than previously possible and the latter provided an opportunity for chromospheric observations of improved height resolution. The altitude, which varied between 16,200 and 17,700 m, freed the observations from the usual weather problems and greatly reduced atmospheric absorption and sky noise in regions of the infrared.

THE Concorde took off from Las Palmas in the Canaries, intercepted the eclipse over Mauritania, paced the umbra along a great circle path over Mali, Algeria, Niger and part of Tchad, and landed in Fort Lamy. The astronomical requirement of stable flight throughout both a maximum period of totality and the second and third contacts (natural contacts) imposed a rigid schedule on the Concorde. Had the aircraft been 2 min early on arrival in the eclipse path, the period of totality would have been reduced by 25 min and one natural contact would have been lost. On the day of the eclipse the Concorde took off and intercepted the umbra within 5 s of the allotted times after 45 min of flight; it maintained maximum ground speed (544 m s^{-1}) (Mach 2.00 to 2.10) throughout the observations and the duration of totality was determined by meteorological conditions in the stratosphere. (We note that the exact definition of second and third contact may have to be re-examined when

the transit of the Moon is very slow.) There was no interference with ground sites and observers. All this is a magnificent achievement on which we congratulate Captain Turcat and his crew.

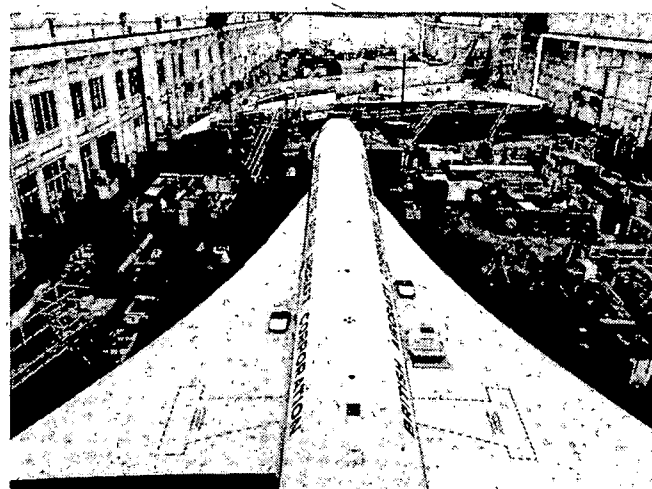


Fig. 1 A view of the aircraft, showing the four special purpose windows on the top. From front to back: crystal quartz window, composite Irtran-2 window, two fused quartz windows. (Picture by Aérospatiale.)

The Concorde carried equipment for experiments by five groups. The instruments and their performance are discussed in the following sections. Apart from four window assemblies, which were mounted in the roof (see Fig. 1), the aircraft required no structural modifications as the equipment was attached to the standard floor tracks. The limitations on space and weight were not severe. The Concorde was made available for five test flights before the eclipse including three Sun-tracking flights. During the eclipse itself the stability of the aircraft was excellent: pitch $\leq 0.1^\circ$, roll $\leq 0.5^\circ$ (peak-to-peak values). An unusual

problem was that, during the eclipse, the attitude of the Sun varied from 27° below zenith ahead of the aircraft to nearly overhead and then to 23° below zenith behind the aircraft.

Here we describe the five experiments, going from the front to the back of the aircraft's cabin.

Far Infrared Emission from the Chromosphere

The purpose of this experiment (Queen Mary College, London) was to examine the upper chromosphere using its emission between $300\ \mu\text{m}$ and $1,500\ \mu\text{m}$. An eclipse gives a necessary condition for this observation, for only lunar occultation of successive layers can produce the required angular resolutions, of order 1 arc s. The best that can be done outside eclipse is around 40 arc s using a large telescope such as the 36-foot NRAO dish at Kitt Peak, because of diffraction limitations. Further, the effective slowing down of the Moon's passage by a factor of ten, enables a high enough signal to noise ratio to be obtained to use the angular resolution available. A final advantage of using the Concorde was that at heights of over 50,000 foot, well above the tropopause, radiation between $300\ \mu\text{m}$ and $1,000\ \mu\text{m}$ reaches the equipment almost unaffected by absorption due to the water vapour rotational spectrum. At ground sites, the average transmission in this wavelength range is only a few per cent.

Our equipment comprises a Rollin InSb photoconductive detector, cooled to liquid He temperature, with useful detectivity between $250\ \mu\text{m}$ and 2 mm. This was fed by a conventional Michelson spectral interferometer, having a $50\ \mu\text{m}$ thick melinex beamsplitter, and 6-cm diameter plane reflectors. The interferometer could be switched to scan through a path difference of 2 cm in 1 s, giving audio output frequencies between 10 Hz and 80 Hz, or ten times more slowly. In the former case analogue Fourier transformation could be performed with suitable electrical filter networks; in the latter digital transformation is needed, to obtain the spectrum of the radiation. The interferometer was fed by an image of the whole eclipsed disk, through a chopper at 1 kHz, used in conjunction with a phase sensitive detector at the output of the radiation detector. Optically the system was very simple: the solar beam passed through the aircraft window, a disk of single crystal quartz, 12 cm in diameter chosen for its transmission properties. It was folded with several plane mirrors on to a lens of TPX plastic, also of high far infrared transmission, into the interferometer. One of the plane mirrors had to be moved electrically at a pre-calculated nearly linear rate along the aircraft axis during totality. A second was guided about the roll axis electrically, using a servo circuit linked to the inertial navigation system of the aircraft, and about the pitch axis manually. A small optical telescope aided the guiding, fed by a 2-cm flat, through which the observer could see the eclipse and surrounding coronal light. Invaluable help was given in designing and constructing the equipment by the National Physical Laboratory Electrical Science division, by the Science Research Council's Culham Laboratory, and particularly by the Radio and Space Research Station, Slough.

The experiment can be counted a success, in that all the individual systems worked, and data were obtained on chart and magnetic tape. Preliminary analysis of the data is consistent with emission detected from the chromosphere, of the right intensity compared with the lunar far infrared signal, and covering the correct angular range outside the lunar disk. The chromospheric signal seems to have been detected not only during the 7 min before photospheric second contact (onset of totality) and 12 min after third contact, but for some 5 min after second and before third contacts.

Infrared Emission of the Thermal Corona

The aim of this experiment (Observatoire de Meudon) was to assess the emission of the thermal corona, or dust corona, in the wavelength range 2 to $13\ \mu\text{m}$. The main advantages of mounting it onboard Concorde are: (i) better atmospheric transmission at 17,000 m; (ii) correspondingly reduced fluctuations of the atmospheric emission which seem to have hampered ground observations at the 1970 Mexican eclipse; (iii) longer integration time.

The window assembly consisted of a circle of four Irtran-2 disks, each of clear diameter 10 cm, with a 3-cm fused quartz window at the centre for guiding purposes. All the optics were mounted on a sliding table, shock-mounted to the floor, to follow, without vignetting, the apparent motion of the Sun in the aircraft. A gyro-heliostat, provided by NASA, stabilised the image on an off-axis, 50 cm diameter, $f/3$ telescope. Image acquisition and scanning were achieved manually by visual control of the image in the focal plane. Differential modulation in this plane switched two diaphragms, 4.4 arc min in diameter, 22 arc min apart in order to balance instrument emission. The beam was divided into three measurement channels, covering respectively 2 to $3\ \mu\text{m}$, 4 to $5\ \mu\text{m}$, 8 to $13\ \mu\text{m}$. The detectors were respectively liquid N_2 cooled InSb photoconductors and liquid He cooled Ge-bolometer.

All three channels could be operated either wide band, or with spectral resolution of about 50 provided by a grating or by a filter wheel (8 to $13\ \mu\text{m}$ channel). Data, including various parameters on board, were recorded both in analogue and in digital form. Total weight of the experiment was about 400 kg.

All the subsystems performed properly during the flight, and the Moon+corona acquisition proved easy. Tracking stability stayed better than 1 arc min for most of the flight. Fifty-six minutes were devoted to wide band scans along and perpendicular to the ecliptic, from 3 to 8 solar radii. Eighteen minutes were devoted to spectral scans at 3.9 solar radii (the area of maximum emission at $10\ \mu\text{m}$).

The radial scans should allow confirmation of previous results at shorter wavelengths, to correlate the longer wavelength emission with them, and hopefully to throw some light on particles material identification through their emission spectra in the $10\ \mu\text{m}$ band.

Invaluable help in building the equipment was provided by the Laboratoire de Physique Stellaire et Planétaire and the Services des Prototypes, both CNRS Institutes, by the Centre National d'Etude des Télécommunications and by Kitt Peak National Observatory.

Photographic Study of the Corona

The experiment (Institut d'Astrophysique de CNRS, Paris) aimed to measure the lifetime of typical structures in the inner corona ($r < 1.5 R_\odot$), to search for oscillatory motions, and to study the outer corona ($r < 15 R_\odot$), by photographic photometry. Three cameras were mounted on a manually oriented gimbal, observing through a fused quartz window 135 mm in diameter. Respective focal lengths are: 180 mm, 1,520 mm, 3,000 mm. Kodak Recording 247S, TRI-X-P and Ektachrome EF films were used. Results on the three systems are as follows.

(1) Several photographs at wide field exposed at 1/30 and 1/60 s; sky brightness appears very low at 17,000 m and should allow a study of the corona at large distances.

(2) Thirty-seven photographs $60 \times 60\ \text{mm}$, 2 min apart, on the 3 m camera, 1/60 s exposure; resolution is of the order of 2 arc s. (Some of these are shown in Fig. 2.)

(3) Two hundred and thirty colour photographs (24×36 format), on the 1.5 m camera. The black and white photographs are calibrated.

Structural changes in the corona are noticeable at the poles, as well as in a coronal enhancement on the eastern side. Photometric study of the films should allow a determination of the lifetime of the polar plumes and an investigation of relaxation processes in the inner corona. Propagation of a coronal wave at the W limb and at about $1 R_{\odot}$ from the limb may be studied. The high spatial resolution should allow investigation of the effect of a supersonic shock wave on the wave front, and thus on the image quality.

High Resolution of the Emission Line Corona

These observations (University of California, Los Alamos Scientific Laboratory, Los Alamos) had two purposes; (1) to determine whether the mechanical periodicities of 5 min observed in the photosphere contribute to the heating of the corona; (2) to use the slow motion shuttering of the solar atmosphere by the lunar limb to observe the development of the emission corona just above the chromosphere.

If the corona-chromosphere transition is about 1,000 km thick, this latter observation would be completed in about 3 s for an observer at a ground site while on Concorde about 30 s were available.

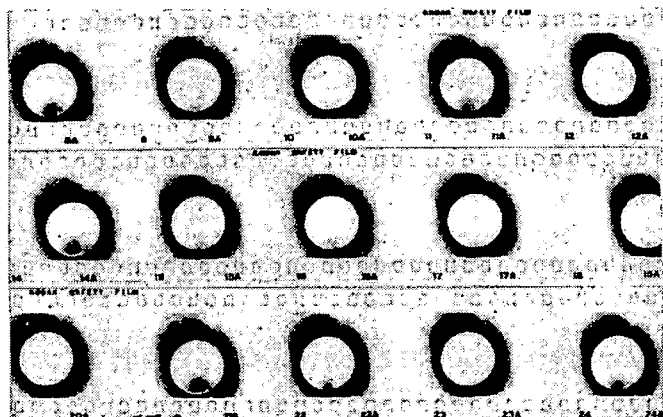


Fig. 2 Successive photographs of the solar corona, taken with $f=3$ m every 20 s, exposure 1/60 s. (J. Begot, Institut d'Astrophysique.)

A single 10-cm fused silica window was left uncoated because of the large altitude change of the Sun during totality. Close to this window a two-axis mirror was located to direct the light into a telescope of aperture 7.6 cm and focal length 1 m. The mirror was guided from photoelectric error signals produced on a tracking focal plane by splitting off 10% of the light from the main beam. The long focal length and consequent large f number was used to obtain a good image scale so that resolution to 10 arc s was available. The main beam was recollimated and passed through an interference filter with a square pass band about $9 \text{ \AA}$ full width at half intensity points. Then spectral scanning through the $\lambda 5303$ emission line was accomplished with a pressure scanned Fabry-Perot interferometer. The image was reformed without change in magnification onto the image intensifier surface optically linked to the vidicon tube. A video frame was obtained every 20 ms and the interferometer finesse, about 50, and scan rate, were adjusted to give 0.5 mm ($0.05 \text{ \AA}$) resolution. Digitisation and subsequent analysis as previously used will be accomplished at Los Alamos. This detailed spectral study was complementary to the successful observations in other coronal emission lines carried out by

other Los Alamos scientists on the NC-135 that was passed by the Concorde near the mid-eclipse point. The instrument weighed about 250 kg.

The main objectives of the observations were achieved. Good spectral line profiles were obtained, and the relative intensity calibration on the video recording will give reliable detection of periodic intensity changes. Although some tracking difficulties were encountered with the photoelectric tracker during the eclipse, adequate tracking was obtained during totality and around third contact to give emission line profiles for both the above purposes.

Particularly striking to the observer was the very dark sky on which a brilliant blue white corona was superposed like a cameo. Near third contact the emergence of the red (hydrogen line-emitting) chromosphere was particularly beautiful as the chromospheric crescent protruded from behind the lunar limb and spread around about a quarter of the solar circumference before the photosphere emerged to end totality. Of course the corona could be seen well after third contact and up to the time we turned away to land at Ft Lamy.

Near Infrared Emission of the Upper Atmosphere

A two-channel spectrophotometer (University of Aberdeen) was used to study the infrared atmospheric system of molecular oxygen in emission. Interference filters with peak transmissions close to $1.27 \mu\text{m}$ and $1.58 \mu\text{m}$ were tilted by motor-driven cams to give spectral scans approximately $0.04 \mu\text{m}$ in range every 60 s. The widths of the passbands of the filter were $0.007 \mu\text{m}$ and $0.01 \mu\text{m}$ respectively. The spectrophotometer was placed close to a passenger window towards the rear of the fuselage in a mounting that permitted selection of the elevation angle of the field of view between 0° (horizontal) and 40° .

The regular dayglow at $1.27 \mu\text{m}$ and $1.58 \mu\text{m}$ was observed during all flights and good measurements of the $1.27 \mu\text{m}$ emission were obtained throughout the total eclipse. The $1.58 \mu\text{m}$ emission disappeared into noise before third contact but was seen clearly before second contact. Observations were obtained at a number of differing elevation angles during totality as well as during the test flights and it is clear that the data will yield estimates of (a) the intensities of the two emission radiances and their ratio; (b) the effective atmospheric absorption of the $1.27 \mu\text{m}$ emission; (c) the effective quenching rate for the $^1\Delta_g$ excited level of O_2 ; (d) the variation with latitude of the $1.27 \mu\text{m}$ emission radiance; and (e) the lack of medium-scale irregularities in the dayglow radiance.

The full results of the individual experiments will be published by the various participating groups; but it is already worth pointing out how profound a change in eclipse observations has accompanied the advent of supersonic aircraft, which has proved to be a very successful carrier in this particular project. There can be no doubt that future plans should favour this method over more conventional approaches.

The project was made possible through the French Délégation Générale à la Recherche Scientifique et Technique and was coordinated by the Institut National d'Astronomie et de Géophysique of the Centre Nationale de la Recherche Scientifique with the full support of the Aerospatiale Company. French experiments were supported by the Institut National d'Astronomie et de Géophysique, British experiments were supported by the Science Research Council and the United States experiment by the National Science Foundation.

Mr Ravaut provided invaluable help during all the flights.

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Geomorphological Dating of Cave Openings at Makapansgat, Sterkfontein, Swartkrans and Taung

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Cave opening at several of the South African hominid sites occurred through incision and valley widening in one current erosion cycle. Measurements of rates of cyclic nickpoint migration and valley flank recession make possible time-place transpositions, and the approximate date of cavern opening can be determined for each site. In each case this date represents a *terminus post quem* for the accumulation of hominid-bearing deposits.

ABSOLUTE dating of the early hominid cave deposits in South Africa has long been of concern to anthropologists, because unresolved problems of taxonomy and phylogeny stem largely from a lack of comparative chronological data for these sites. In particular, the chronological position of *Australopithecus africanus* remains in doubt. Faunal assemblages from the South African sites are often too restricted in their range of species to permit correlations either between sites, or with dated assemblages from East Africa.

Although radioisotopic and other techniques have been applied to the South African sites no absolute dates have been obtained. I therefore set out to investigate the possibility of applying geomorphological techniques of age determination in the hope that these might throw light on the date of accumulation of the South African cavern deposits.

Erosion Cycles

The method is based on a quantitative assessment of rates of cyclic erosion relative to well-established geomorphological datum levels. Since the Jurassic the African continent has been subject to five active episodes of epeirogenic movement, separated by intermissions in which erosion has advanced inland from the coast, with concomitant sedimentation of the continental shelf. The ages of these movements and the resulting offshore deposition are well known on the basis of both tectonic and marine palaeontological studies¹⁻⁵.

The recurrent pattern of continental landform development which succeeded each active episode has been the subject of detailed analysis^{6,7}; it is significant that recession of valley nickpoints inland from the coastal margin was

followed by valley widening, scarp retreat and pedimentation, leading ultimately to the formation of gently undulating pediplains or erosion surfaces. Where such surfaces have reached an advanced stage of planation local relief is minimal, and their distribution may be mapped very accurately. In some areas such as the South African Highveld, these plains extend unbroken for thousands of square km, and transgress both structure and lithology without interruption. Their existence in the African landscape is irrefutable, and their distribution has been described and mapped by several workers^{2-4,7-12}.

The erosion cycles seen near the South African hominid deposits are the African and Post African I. The most recent (Plio-Pleistocene) cycle is represented over much of South Africa by gorges incised into the coastal hinterland, and advanced planation referable to it is restricted to local basins. The date of inception of these cycles, based on palaeontological studies of the equivalent marine sediments, is as follows:

Table 1 Erosion Cycles in South Africa*

Cycle	Marine depositional equivalent	Date of inception
African	Littoral Senonian strata of east coast, with succeeding Eocene in Mocambique; Late Cretaceous and Eocene strata of Angola	Mid-Cretaceous (100 m.y. BP)
Post African I	Burdigalian marine series	Miocene (20 m.y. BP)
Plio-Pleistocene	Red "Berea" and other coastal sands	(2 m.y. BP)

* Adapted from King³.

The African erosion surface is characteristically well planed and provides a readily identifiable datum level in all areas unconsumed by later incision; however, local deformations along well defined axes are present, and are related to the tectonic disturbances which initiated the Plio-Pleistocene incision¹³. One such axis coincides with the Continental divide along the Witwatersrand ridge some 30 km to the south of the Sterkfontein and Swartkrans sites, and has resulted in upwarping of the African surface evident in the marked northerly tilt of discontinuous benches eroded in this cycle along the upper flanks of the Bloubaan Valley. Here African benches decline in elevation downstream at approximately 6 m km⁻¹.

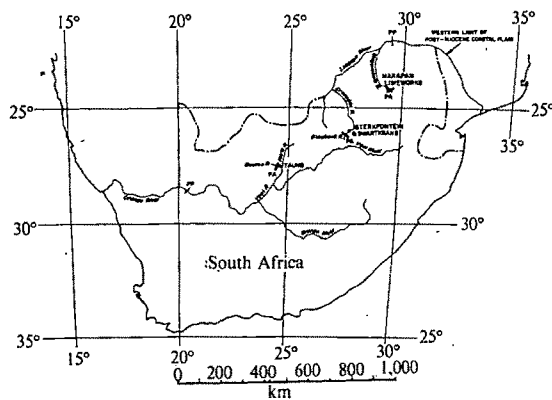


Fig. 1 Map of South Africa showing hominid sites, drainage systems and nickpoints referred to in text. ●, Hominid sites; PP |, Plio-Pleistocene nickpoint; PA ||, Post-African nickpoint.

Nickpoint Migration

Figure 1 shows the locations of the sites and drainage systems which I discuss. The positions of the African, Post-African I and Plio-Pleistocene nickpoints, which represent the furthest point reached by incision in each cycle, are indicated relative to the streams concerned. In every case the hominid site is situated in a valley incised below the African erosion surface in the Post-African erosion cycle; valley or cave opening therefore occurred under the influence of this incision.

Figure 2 provides a graphical representation of the rate of nickpoint migration inland from the coast expressed as a proportion of the total stream length. The rate of nickpoint migration has been calculated by measuring the length of the stream channel segments affected by the Plio-Pleistocene and Post-African I incision. The mean rate of nickpoint migration was then plotted in relation to that proportion of the channel length represented by the mid-point of each segment, taking into account the position of the coast at the time of inception of the cycle which produced the nickpoint concerned. In the absence of supplementary evidence, it was assumed that the nickpoint migration rate between each of these points was subject to a linear decline culminating in zero at the point of origin of the stream in the watershed area.

This assumption is, of course, erroneous in that nickpoint migration rates are undoubtedly influenced by variations in lithology, climate, tributary flow and sediment load. Most of these influences are not, however, susceptible to quantitative assessment, although reference to Table 2 shows that the lithological composition of the valleys is comparable in each basin. Hence lithological modifications of the linear relationship are likely to be generally equivalent in each case. Moreover the errors in the use of the linear interpolation technique are likely to be reduced greatly by the close proximity of each site to the headwater of the local stream (see Fig. 1). In no instance does this exceed 14.24 km or 2.71% of the channel length, and migration rates so near to the stream source are so low, owing to the small available erosive potential, as to be little affected by possible departures from the linear mode of decline.

The nickpoint migration graphs presented in Fig. 1 demand some comment. Reference should be made to Table 3 in which the measurements from which the graphs have been constructed are presented. The graphs are numbered 1, 2 and 3 to indicate the drainage systems concerned: (1) the Limpopo-Magalakwin-Makapan drainage system, containing the Makapansgat limeworks site (*a*); (2) the Limpopo-Crocodile-Bloubank drainage system, containing the Sterkfontein and Swartkrans sites (*b*); (3) the Orange-Vaal-Harts-Buxton drainage system, containing Taung site (*c*) at the Buxton lime quarry.

Table 2 Occurrence of Various Lithological Types in Drainage Basins

Rock types	% of total channel length in drainage basins		
	1*	2*	3*
Moderately resistant Palaeozoic and Mesozoic sediments	30.25	29.43	27.06
Resistant Precambrian basic igneous rocks, largely plutonic	2.52	3.65	1.65
Resistant Precambrian acid igneous rocks and gneisses, largely plutonic	38.23	44.00	36.93
Very resistant Precambrian sediments and meta-sediments	29.00	22.92	34.36

* Drainage basins: 1, Limpopo-Magalakwin-Makapan; 2, Limpopo-Crocodile-Bloubank; 3, Orange-Vaal-Harts-Buxton.

The lower reaches of drainage systems (*a*) and (*b*), below the Magalakwin-Limpopo confluence, are common in the lower course of the Limpopo river, which enters the Mocambique coastal plain just to the east of the South African border. This plain is largely underlain by marine sediments, and was elevated to its present position by post-Miocene movements⁶. For this reason the segment of the Limpopo channel crossing it was ignored in measuring the extent of Post-African I nickpoint recession from the coast.

All three graphs are of similar form with a conspicuous inflection indicating substantially different rates of nickpoint

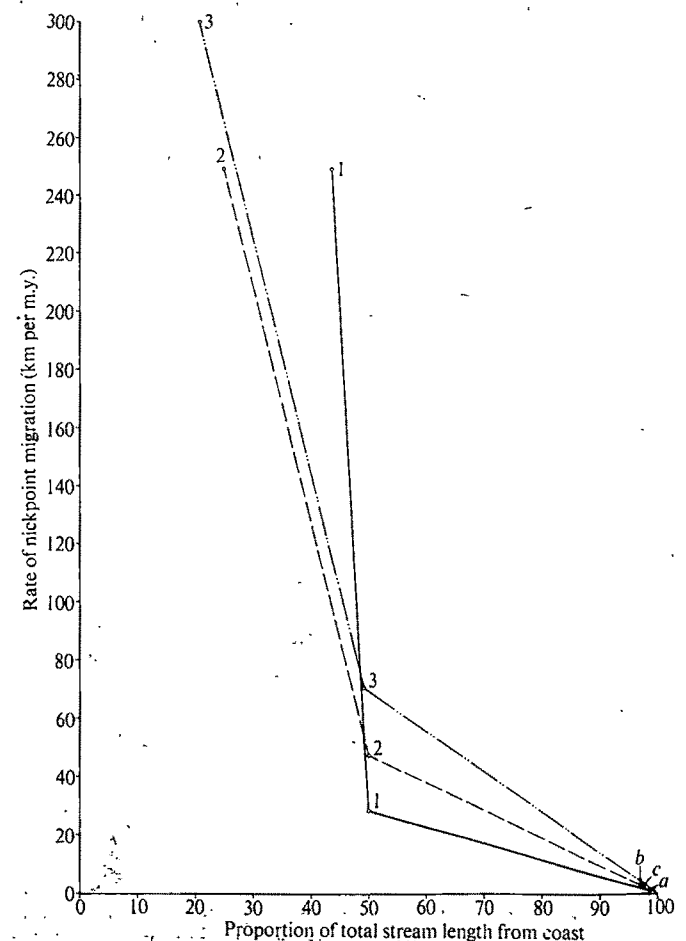


Fig. 2 Rate of nickpoint migration inland from coast. Sites, *a*, Makapansgat limeworks; *b*, Sterkfontein and Swartkrans; and *c*, Taung. Drainage systems: (1) Limpopo-Magalakwin-Makapan; (2) Limpopo-Crocodile-Bloubank; and (3) Orange-Vaal-Harts-Buxton.

migration in the Post-African I and Plio-Pleistocene erosion cycles. The more rapid rate of recession in the Plio-Pleistocene cycle is undoubtedly the result of the greater magnitude of the associated uplift and warping of the continental margin. Variations in rates of nickpoint migration between the different drainage systems may be explained by differences in the degree of stream activity, as dictated by volume and regularity of flow. Hence the lowest rates are evident in the Limpopo-Magalakwin-Makapan system which is non-perennial over much of its length, and the highest rates occur in the Orange-Vaal-Harts-Buxton system, which is subject to a more regular flow, particularly below the Vaal-Harts confluence.

From these measurements it is possible, to determine the mean rate of nickpoint migration between each site and the current position of the Post-African I nickpoint, which is situated in each case a short distance upstream. In all drainage basins this channel segment is contained almost entirely within the lower part of the Dolomite Series, Transvaal System, so that the calculated migration rates should not involve errors caused by major lithological variations. Division of this distance by the mean rate of nickpoint migration associated with it, gives the date before present of the arrival of the Post-African I nickpoint opposite each site. These dates are given in Table 3. They merely provide, however, a *terminus post quem* for the valley deepening and widening during which cavern opening occurred, or the locale was created for the accumulation of the hominid-bearing deposit. In order to determine the further time lapse required for this to occur it is necessary to consider briefly the geomorphological environment of each of the sites.

Analysis of Cave Sites

All of the deposits occur at similar stratigraphic levels within the Dolomite Series, which consists of interbedded

horizons of soluble dolomite and insoluble chert. This rock is subject to cycles of solution and cavern development closely linked to the cycles of subaerial erosion described previously^{10,11}. After the solutional formation of a cavity beneath the water table, incision and reduction of local base level produced lowering of the phreatic surface; concomitant valley widening caused the land surface to intersect the cavity creating an opening to the surface, commonly through a vertically enlarged joint or aven. This opening permitted the ingress of externally derived hillside soil, as well as hominids and animals. Hence, to determine the date of the earliest accumulation of the cave deposit, it is necessary to determine the time period which elapsed between arrival of the new erosion cycle opposite the site and recession of the valley side to a point at which cavern opening occurred.

The situation described above pertains in the case of the Makapansgat Limeworks, Sterkfontein and Swartkrans deposits, but the Taung deposit accumulated in cavities developed in a series of calcareous tufas deposited on the valley flank at Buxton subsequent to the incision of the valley in the Post-African I erosion cycle¹⁴. Hence the geomorphological controls governing cavern opening do not apply in this case, and all that may be deduced is that the hominid-bearing deposit post-dated the arrival of the Post-African I nickpoint (0.87 m.y. BP).

In the case of the dolomite cavern deposits, the time lapse involved in the widening of the valley to produce cavern opening has been calculated as a proportion of the total valley widening in the Post-African I cycle that has occurred to date. Figures 3 and 4 show topographic sections through the Makapan and Bloubank valleys at the limeworks, Sterkfontein and Swartkrans site, together with the local elevations of the African erosion surface. These elevations were determined through the construction and superimposition of numerous transverse and longitudinal profiles over large areas in the vicinity of each site. Both valleys are composite, in that they have been incised in both the

Table 3 Nickpoint Recession

Drainage system	Total trunk channel length (km)	Headward recession of cyclic nickpoints Distance from coast (km)	% of total channel length	Rate of recession (km per m.y.)	Distance of site from coast as % of channel length	Distance of oldest upstream nickpoint from coast as % of channel length	Mean rate of recession between site and oldest upstream nickpoint (km per m.y.)	Distance between site and oldest upstream nickpoint (km)	Date in m.y. BP of arrival of oldest nickpoint opposite site	Proportion of total valley down-cutting and widening (%) in locally current erosion cycle required to open cave	Date in m.y. BP of cave opening
Limpopo-Magalakwin-Makapan	570.15	Plio-Pleistocene: 497.80 Post African I: 566.21	87.30 99.28	248.90 28.36	Makapansgat limeworks: 98.78	99.28	0.55	2.86	5.24	30.00	3.67
Limpopo-Crocodile-Bloubank	960.77	Plio-Pleistocene: 497.80 Post African I: 949.08	51.81 98.77	248.90 47.45	Sterkfontein: 97.29 Swartkrans: 97.40	98.77	1.85 1.79	14.24 13.12	7.71 7.33	57.77 64.91	3.26 2.57
Orange-Vaal-Harts-Buxton	1,436.46	Plio-Pleistocene: 596.90 Post African I: 1,408.83	41.58 98.11	298.45 70.45	Taung: 97.94	98.11	2.73	2.38	0.87	—	<0.87

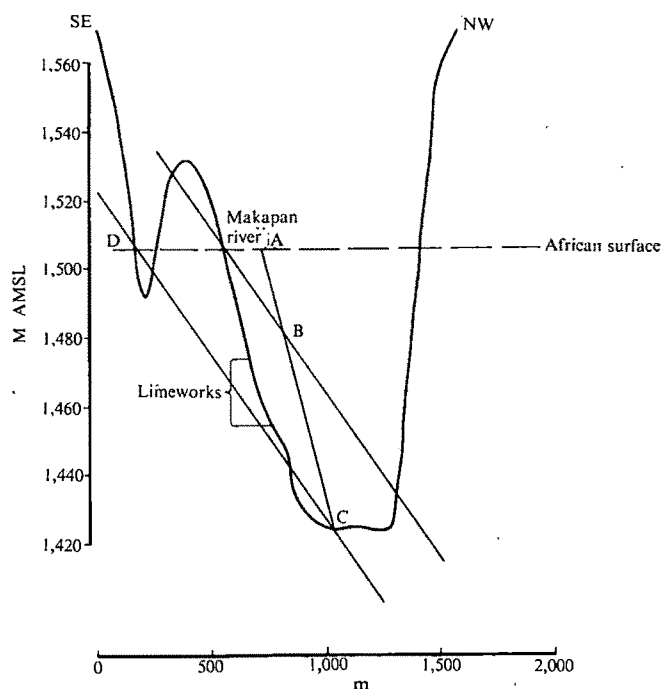


Fig. 3 Section through Makapan Valley at limeworks (see text for explanation).

African and Post-African I erosion cycles, but the presence of benches, whose projected elevations accord with one another and with nearby areas of African planation, leave no doubt as to the portion of the incision referable to the Post-African I cycle.

To determine the approximate time required for valley widening to open the caverns, a line was drawn between the base of the present stream channel and the point of intersection of the African surface with the present valley side (line CD). A parallel line was drawn through the projected apex of the aven through which cavern opening occurred, and another was inserted to indicate the downward path of the stream channel during its incision from the African level to its present position (line ABC). It should be noted that these latter lines are not vertical, but assume varying inclinations in the three sections. This reflects lateral channel migration during the course of incision, partly in conformity with the local dip of the dolomite strata, partly as a result of asymmetrical downcutting in relation to the slip-off and undercut slopes of incising meanders. The original position of the channel at the level of the African surface was carefully determined in each case from distributions of benches and terraces occurring at this and subsequent levels.

The intercept AB is a measure of the amount of incision and valley widening required to open the cavern. This, expressed as a proportion of the total incision along the downward path of the channel (AC), represents that proportion of the time which elapsed subsequent to the arrival of the Post-African I nickpoint opposite the site, required to achieve cavern opening.

In this analysis of valley widening several assumptions have been made: first, that the valley flanks approximated to a rectilinear configuration during recession; second, that the downward path of the channel during incision was rectilinear; and third, that both channel incision and concomitant valley flank recession occurred at a regular rate. None of these assumptions is likely to be wholly accurate. The probable departures from these ideal conditions are, however, unlikely to have been sufficiently great to affect the relative dates or the general order of ages indicated in the

results, particularly because incision and valley widening occurred in very similar sedimentary successions at each site.

The proportions of valley flank recession required to open each cavern are presented in Table 3, and the resulting date for the first opening of each to permit the ingress of hillside materials, hominids and animals is given. These are approximately 3.7 m.y. for the Makapansgat limeworks, 3.3 m.y. for Sterkfontein, 2.6 m.y. for Swartkrans, and, as has been indicated previously, somewhat less than 0.87 m.y. for Taung.

Implications

These ages for the first opening of caverns or locales for the accumulation of hominid-bearing deposits embody certain errors inherent in the assumptions made during their derivation. It is, however, considered unlikely that they are large enough to affect the relative dates or general order of ages that have been deduced for two reasons: first, the lithological compositions of the channels are generally similar in each basin, and almost identical between each site and its upstream nickpoint; hence possible error factors caused by lack of lithological homogeneity are likely to be fairly evenly spread relative to the various sites. Second, interpolations for valley downcutting and widening at each site have been carried out relative to the actual profile of the valley section; hence local erosional irregularities have been considered.

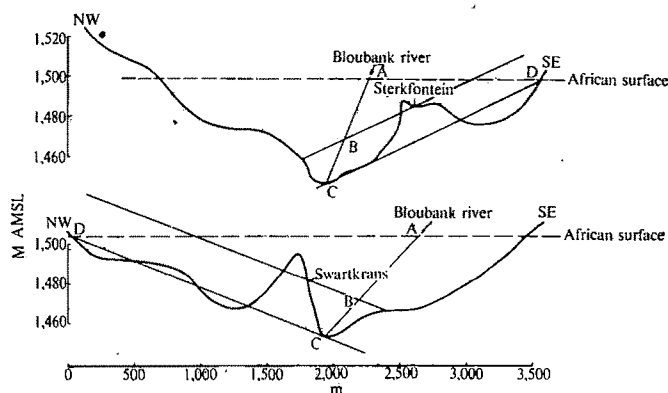


Fig. 4 Sections through Bloubank Valley at Sterkfontein and Swartkrans (see text for explanation).

Comparisons of faunal material from all sites, and the remains of *Australopithecus robustus* from Swartkrans, with similar dated material from East Africa, have suggested that the deposits at Makapansgat limeworks, Sterkfontein and Swartkrans may be at least 0.5 m.y. younger than is indicated by the dates presented here^{15,16}. It should, however, be borne in mind that these dates are for the earliest cave opening, and that strata may be present in the lower levels of the deposits which are older than those from which the comparative material was derived. Such early strata of substantial thickness have recently been recorded both at Makapansgat and Sterkfontein. Furthermore, as Butzer¹⁷ has pointed out, the local production of hillside soil which forms the bulk of the breccias is extremely slow, and tens or even hundreds of thousands of years may have been required for such extensive deposits to accumulate. The young date for the Taung site is somewhat surprising, although Wells¹⁸ has suggested, on faunal grounds, that the accumulation of the Taung hominid deposit may have occurred later than was previously thought.

I hope that, in the absence of suitable isotopic dating methods, these results may provide less precise interim data until other chronometric techniques are developed.

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agement. This article was adapted from the Chairman's address to Witwatersrand Centre, South African Archaeological Society, delivered February 28, 1973.

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Implications of the New Age Estimates of the Early South African Hominids

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Divergences exist between recent faunal and geomorphological estimates of the age of several South African australopithecine sites. New stratigraphic evidence from Sterkfontein and Makapansgat suggests a lengthy lapse of time between cave opening and deposition of dated fossil bones, and thus provides a basis for explaining the apparent discrepancies. The young date inferred for the Taung skull makes it up to 2 m.y. more recent than *Australopithecus africanus* from the Transvaal caves. As Taung is clearly not a member of *Homo erectus*, it is reasonable to hypothesise that it may be a later survivor of *A. robustus*.

UNTIL very recently, a lack of 'absolute' or of radiometric dates for the South African early hominids has vitiated any attempt to achieve a reliable synthesis between the South and East African early hominid lineages. Faunal comparisons, often based on rather inadequate fossil assemblages, had indicated two broad groups of fauna—an earlier group, known formerly as the Sterkfontein Stage^{1,2} and subsequently as the Sterkfontein Faunal Span³, and a later group, the Swartkrans Stage, renamed the Swartkrans Faunal Span. The term faunal span was introduced to connote both a particular faunal assemblage and the temporal duration of its existence. The faunas from Sterkfontein, Makapansgat and Taung had been provisionally assigned to the earlier span and those of Swartkrans and Kromdraai to the later span^{4,5}.

Up to the middle nineteen-sixties, these intraregional faunal comparisons had led to the view that the South African sites could be arranged, from oldest to youngest, as

follows: Taung→Sterkfontein→Makapansgat→('Sterkfontein Extension Site')→Swartkrans→Kromdraai.

Wells has, however, doubted for some time^{5,6} whether the faunal evidence justifies the view that Taung with its type specimen of *Australopithecus africanus* is indeed the earliest South African australopithecine site. The hominid-associated fauna could just as readily be equated with that of Swartkrans or even of Kromdraai: and most of the identified faunal elements belong to parts of the Taung deposit which is appreciably older than the *Australopithecus breccia*. The latest check-list of cercopithecoids⁷ shows the significant absence from Taung of *Parapapio broomi*—which is the commonest cercopithecoid at Makapansgat and Sterkfontein. Moreover, there are two species of *Papio* at Taung, another two at Kromdraai and one at Swartkrans, but none at Makapansgat or Sterkfontein. It would certainly seem that the primates in the Taung cercopithecoid breccia are younger than those of the Sterkfontein Faunal Span. The analyses of Peabody⁸ and Butzer⁹, in turn, agree that the cercopithecoid breccia is appreciably older than the *Australopithecus breccia* at Taung: Butzer places them in two successive phases of one geomorphological cycle, namely Norlim 2 and 3. So the Taung hominid is younger, by a still greater margin, than the Sterkfontein Faunal Span.

Until 1970, the seriation of South African early hominid sites was based on such purely relative faunal dates. Meantime, faunal successions in East Africa were being calibrated with some precision by suites of potassium-argon dates. The next logical step was to attempt indirect dating of the South African sites by correlation of their faunas with the well-calibrated lineages of East African fauna. This was first attempted by Cooke¹⁰, who provisionally suggested that the Sterkfontein and Makapansgat breccias may be about twice as old as has hitherto been thought, possibly "in the vicinity of 2.5 to 3.0 million years old". This was based on a comparison of the fossil suids from both South African sites and of *Elephas recki* from Makapansgat (*contra*¹¹) with their well-dated counterparts from East Rudolf and Omo (Shungura Formation). Cooke's view is supported by Maglio¹², who feels that although the faunal evidence is far from adequate and further studies are needed, both Maka-

pansgat and Sterkfontein seem to correlate best with the East African faunal succession of about the middle Shungura and lowest Koobi Fora formations^{13,14}. In terms of absolute chronology, Maglio believes that 2.5 m.y. is a fair estimate of the age of these faunas. Similarly, Cooke¹⁰ has suggested, on faunal comparisons, that Swartkrans is at least as old as Bed I, Olduvai (~1.8 m.y. for the Upper Member of Bed I). These tentative faunal datings have suggested that the deposits of Makapansgat and Sterkfontein are much older than had been supposed, whereas that of Taung seems to be far younger.

The new geomorphological studies, carried out by Partridge and announced in this issue of *Nature*¹⁵, as well as those of Butzer⁹, have provided the first guarded corroboration of the faunal dates provisionally claimed by Cooke and Maglio. In spite of their use of very different approaches, both Partridge and Butzer have arrived at a relatively young age for the Taung deposit. Moreover, Partridge has provided the first evidence suggesting approximate dates for the opening of the Makapansgat (3.7 m.y.), Sterkfontein (3.3 m.y.) and Swartkrans (2.6 m.y.) caves.

These admittedly conjectural estimates suggest that the Makapansgat cave opened earliest; that of Sterkfontein about 400,000 yr later, and that of Swartkrans, some 700,000 yr thereafter. It has not yet been possible to date the Kromdraai fissure deposits by these methods; Taung would be not older than Swartkrans and Kromdraai on Butzer's analysis, and as young as <0.87 m.y. by Partridge's approach: that is, about 1.0 m.y. younger than Swartkrans.

Partridge's method of dating is still, of course, exploratory and in its application to this problem as yet unconfirmed. Even if the method is still subject to refinement, it may be of value here to examine the degree to which his provisional dates fit other known facts and interpretations. Such a preliminary assay may, indeed, assist in putting Partridge's method to the test.

Makapansgat and Sterkfontein

Non-calibrated faunal comparisons among the South African sites had already led Wells⁶ to infer that some of the many points of difference between the faunas of Makapansgat and Sterkfontein might plausibly suggest that Makapansgat is the older of the two. This inference would now seem to gain support from Partridge's estimates for the opening of the caves, namely 3.7 and 3.3 m.y. respectively.

As has been shown, comparisons with the calibrated fauna of East Africa point to 2.5 m.y. or 2.5–3.0 m.y. for Makapansgat and Sterkfontein. There is thus a discrepancy between geomorphological and faunal estimates of 1.2–0.7 m.y. for Makapansgat and of 0.8–0.3 m.y. for Sterkfontein. It may pertinently be enquired if these are real discrepancies or technical ones. On the one hand, the divergences may be the consequence either of a methodological difficulty or lack of refinement in the geomorphological approach used, or of a problematical correlation, or of an error of faunal sampling. On the other hand, the departure between the two estimates may reflect a long lapse of time between the earliest opening of the caves and the deposition of the fossils which have been correlated with East African lineages.

Recent work at Sterkfontein¹⁶ has demonstrated the existence of an earliest bone-bearing breccia under the thick travertine once regarded as the floor of the main deposit (ref. 17, and unpublished work of T. Partridge, A. B. A. Brink and A. R. Hughes). This breccia may extend downwards for a considerable depth into the underground cave system (personal communication from J. Wilkinson). The accumulation of this lowest breccia followed the opening of the cave, but preceded the deposition of the stratigraphically much higher fauna on which the faunal dating has been based. In other words, the early stages in the

accumulation of the Sterkfontein deposit may have lasted far longer than had been imagined. This new stratigraphic evidence accords well with the lapse of a lengthy interval between the first opening of the cave (estimated at 3.3 m.y.) and the accumulation much higher in the deposit of the fossil bones on which the provisional faunal dating (2.5–3.0 m.y.) is based. Already, Butzer¹⁸ has inferred that "the Transvaal cave fills record, at the very least, several tens of thousands of years . . . and, quite possibly, several hundreds of thousands of years". In the light of this stratigraphic evidence, Partridge's estimate of a date of the order of 3.3 m.y. for the first opening of the cave is not wholly unexpected; nor is it incompatible with the provisional faunal date based on suids.

At Makapansgat, it was until recently uncertain whether there was comparable stratigraphic evidence to support a lengthy interval between the date estimated for the opening of the cave (3.7 m.y.) and the deposition of suid and elephant bones on which the tentative faunal dating (2.5–3.0 m.y.) has been based. During excavations at Makapansgat Limeworks in July 1973, I located a considerably older, lower breccia. In the Lower Cave, a conspicuous sheet of travertine has for long been regarded as lying on the original floor of the cave. Above this travertine is an accumulation of red, water-laid breccias, overtopped by the bone-rich grey breccia (which has yielded most of the hominids and datable fauna), which in turn is succeeded by the cercopithecoid-rich pink breccia, on which lies a surviving scale of the dolomite roof. The fauna used for comparison with the East African suids and proboscideans derives from layers well above the travertine floor. During our most recent excavations, in the lowest-lying parts of the cave, I located a succession of breccias and travertines below the supposed basal travertine; some of these oldest breccias proved to be bone-bearing.

Thus, at Makapansgat, as at Sterkfontein, there is stratigraphic evidence suggesting a lengthy lapse of time between the earliest opening of the cave and the deposition of those bones used for comparison with East African faunas. This evidence would suggest a much older date for cave opening than for the calibrated fauna. Against this background, Partridge's suggestion that the date of cave opening was of the order of 3.7 m.y. is not wholly unlikely; nor does it seriously contradict the faunal date of 2.5–3.0 m.y. tentatively inferred by Cooke and Maglio.

Both at Makapansgat and at Sterkfontein, it now seems not altogether improbable that the filling of the caves may have occupied between 0.3 and 1.2 m.y. The upper part of this range of time is sufficiently long to make it likely that significant changes of fauna and perhaps of culture may be entombed within the deposit. Already there is some evidence to suggest a succession, at both Sterkfontein and Makapansgat.

The earlier age inferred for the Makapansgat deposit seems to be in keeping with the evidence of the hominids themselves. The Makapansgat hominids are characterised by 'gracile' or *A. africanus* features, but include as well some *A. robustus* traits in crania, jaws and teeth, to which attention was drawn in 1967: "In these respects, the Makapansgat specimens seem to show a somewhat nearer approach to *A. robustus* than do the Sterkfontein specimens"¹⁹. This led me subsequently to suggest tentatively that more than one species of hominid is present at Makapansgat^{20,21}. From a study of the mandibles, Aguirre²² has since claimed that the Makapansgat juvenile jaw, MLD 2, indubitably represents a young male *A. robustus*.

In the light of the new tentative age determinations for Makapansgat, it might be suggested that a *mélange* of *A. africanus* and *A. robustus* features might have been expected in an early population of *A. africanus*, close to the point of speciation into robust and gracile species. As an early population, it is reasonable, in Darwinian and in genetic

terms, to suppose that its spectrum of anatomical polymorphisms adumbrates later speciation of the *A. robustus*-*A. boisei* lineage from a basic *A. africanus* lineage.

Swartkrans

The Swartkrans Faunal Span is younger than the Sterkfontein Faunal Span. The Swartkrans fauna itself is considered older than that of Kromdraai and than the Cornelia Faunal Span (from Cornelia, Orange Free State)⁶. Partridge's new study has tentatively inferred a date of 2.6 m.y. for the opening of the Swartkrans cave, and Cooke, on the fauna, has estimated an age of roughly 1.8 m.y. at least. Again there is an apparent discrepancy, this time of about 0.8 m.y., between the two estimates: but both confirm what intraregional faunal comparisons have indicated, that Swartkrans is younger than Makapansgat and Sterkfontein. Brain's excavations at Swartkrans^{23,24} may yet reveal whether there is a stratigraphic explanation for the gap between the two claimed dates at this site.

Taung

The type-site of *Australopithecus africanus*, Taung, was long regarded as the oldest of the South African early hominid sites. Wells pointed out that the species most closely associated with the juvenile hominid skull do not warrant this view, and that Taung could equate with Swartkrans or even Kromdraai^{15,6}.

Butzer and Partridge agree that Taung is much younger than Makapansgat and Sterkfontein, claiming that it is either coeval with or younger than Swartkrans-Kromdraai (Butzer), or younger than 0.9 m.y. BP (Partridge). The second estimate refers to the *terminus post quem* for the formation of the original Taung cavern: on this conjecture, it would follow that the lower, cercopithecoid breccia is somewhat younger than <0.9 m.y., and the upper, *Australopithecus* breccia would be still younger, perhaps 0.8 or even 0.7 m.y. BP. If, as Cooke suggests¹⁰, the age of the Swartkrans fauna is at least 1.8 m.y., Butzer's maximum age for Taung would be 1 m.y. earlier than Partridge's tentative estimate. On the other hand, Butzer agrees that Taung may be younger than Swartkrans—and this would reduce the discrepancy between his and Partridge's estimates. It is not possible at present to determine if any residual discrepancy would have a real, stratigraphic basis, or be only apparent, the result of errors in either or both estimates.

In any event, one can only conclude that, far from being the oldest australopithecine site in southern Africa, Taung is probably the youngest. What is more, it may compete with Chesowanja and Peninj (both just over 1.0 m.y. BP) as being the site of the most recent survival of an australopithecine anywhere in Africa. In Fig. 1, Taung has been plotted at about 0.8 m.y., with an interrupted line extending back to the approximate date of Kromdraai.

On the basis of Partridge's estimate, the Taung skull, the type specimen of *A. africanus*, represented a hominid that lived up to 2 m.y. later than the Makapansgat and Sterkfontein hominids, which are generally regarded as belonging to *A. africanus*. Between the two periods of 2.5–3.0 m.y. and 0.8 m.y., no trace of *A. africanus* has been identified in southern Africa, even though two sites (Swartkrans and Kromdraai) are probably dated to the intervening period. In East Africa, hominids datable to the intervening period have been attributed, in the main, to the robust australopithecines (the superspecies, *A. robustus*/*A. boisei*²⁵) and to *Homo* sp. Furthermore, some workers have claimed to recognise the presence of *A. cf. africanus* at Omo (chiefly isolated teeth) and at Olduvai (for example, Olduvai hominid 7, recognized by Leakey *et al.*²⁶ as the type specimen of the bigger-brained *H. habilis* and regarded by others as *A. habilis*). Thus, the presence of *A. africanus* in East Africa between 2.5–3.0 m.y. and 0.8 m.y. remains disputed and

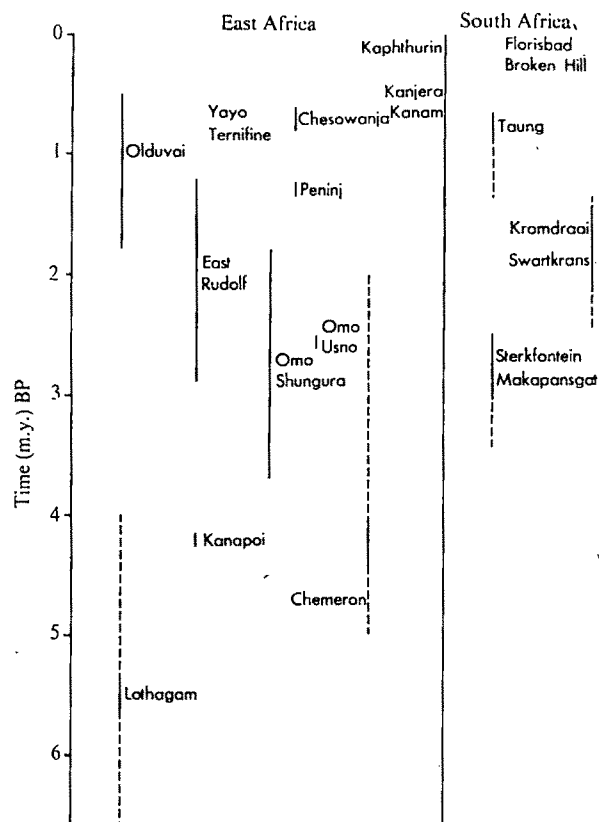


Fig. 1 Provisional temporal distribution of East African hominids (after Maglio¹²) and of South African hominids (based on the new dates).

equivocal. The most convincing East African claimant for membership of *A. africanus* is the far older Lothagam mandible²⁷ dated to about 5.0–5.5 m.y.²⁸.

Phylogenetic Implications

Figure 1 depicts the dates of the South African sites, based on the latest provisional faunal datings and modified somewhat by the geomorphological estimates of Partridge. These are compared with those for East Africa as formulated by Maglio¹².

In Fig. 2, an attempt has been made to represent the various hominid taxa living at 0.5 m.y. intervals in South and East Africa. Although there are several different classifications of hominids, I have used a bigeneric one, because the recognition of two Plio-Pleistocene hominid genera, *Australopithecus* and *Homo*, enjoys the greatest consensus at the present time^{25,29}. Furthermore, I have used a division of *Australopithecus* into *A. africanus*, *A. robustus* and *A. boisei*, the last two being considered as two allopatric species forming one superspecies²⁵; and of *Homo* into *H. habilis*, *H. erectus* and *H. sapiens*.

In Fig. 3 I have made a new reconstruction of the phylogeny of the Plio-Pleistocene hominids, using the new tentative South African hominid age estimates. The early origin of *Homo* in the figure is based on the probable date of 2.9 m.y. for R. E. F. Leakey's new cranium, KNM-ER 1470, found below the KBS tuff of East Rudolf³⁰. From my examination of this important find, kindly permitted by Mr Leakey, I am impressed by the morphological resemblances between ER 1470 and the crania assigned to *H. habilis*. Tentatively, I accept Leakey's attribution of ER 1470 to *Homo* sp.: as a provisional judgment, it may even extend our concept of the range, in time and morphology, of *H. habilis*.

If the late date proposed for the Taung child is more or less correct, its only known contemporaries are *Homo* (most

probably *H. erectus*) and the last-surviving members of the robust australopithecine superspecies (Fig. 2). The inferred date of about 0.8 m.y. BP makes it >1.0 m.y., and probably about 2.0 m.y., more recent than the latest of the other African fossils assigned to *A. africanus*.

Hence, it may well be questioned whether the Taung child does in fact represent *A. africanus*, in the sense in which this taxon is defined from Makapansgat and Sterkfontein. The possibility of isolated relict populations of *A. africanus* having survived in the southerly cul-de-sac of Africa for 1 to 2 m.y. after the species had disappeared elsewhere, or had given rise to the earliest species of *Homo* in Africa, cannot of course be excluded. On the other hand, because its small brain³¹ and its dental characters would exclude it from *H. erectus*, it must seriously be considered whether the Taung child is not a late surviving member of *A. robustus* or *A. cf. robustus*. Although nearly 50 yr have elapsed since its discovery³², it is true to say that the Taung skull has never yet been fully analysed and described. In my laboratory, G. R. Sperber has recently made X rays of the Taung maxilla and mandible which reveal the unerupted permanent premolars and second molars. A careful radiological study of these tooth germs, and the possible extraction of two of them, may provide additional and perhaps diagnostic dental evidence on the affinities of the Taung child. Certainly, the recent discovery of new juvenile specimens of *A. robustus*²⁴ and other early hominids would make a definitive study of the Taung skull both timely and potentially most rewarding. It is hoped that such a study would provide evidence to confirm—or refute—the hypothesis that the Taung child represents a member of *A. robustus*.

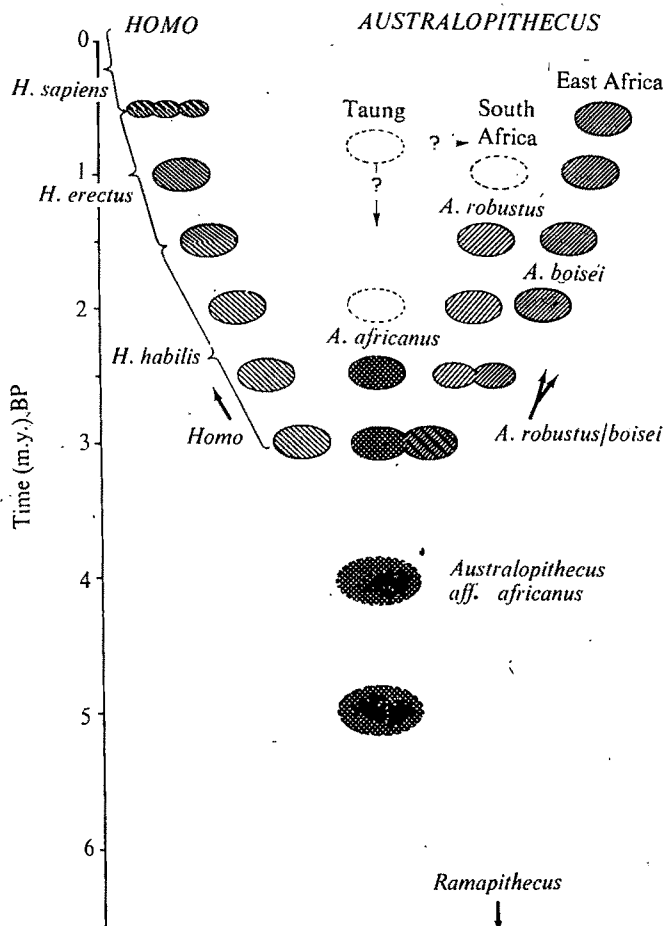


Fig. 2 Hominid populations in Africa at various times in the Plio-Pleistocene. The oval figures at each time level represent the various systematically identified, synchronic hominid taxa living in Africa. The horizontal distance between a pair of ovals at the same time level is roughly proportional to the morphological and taxonomic distance between the populations or taxa represented by the ovals.

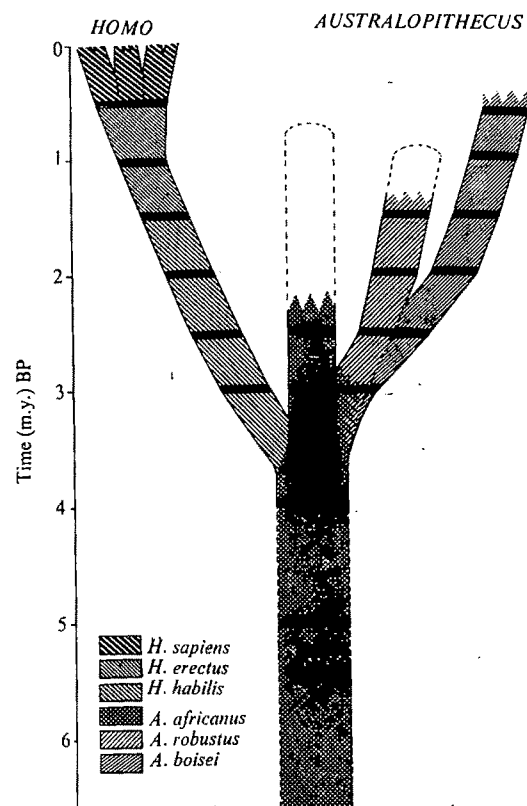


Fig. 3 Provisional phylogenetic tree of the Plio-Pleistocene Hominidae. The possible extension of *A. africanus* and/or *A. robustus* to a very recent period (<1.0 m.y. BP) is suggested as two alternative means of accommodating the Taung skull at its new young date (0.7–0.8 m.y. BP).

Taxonomic Implications

If the Taung skull has to be removed from the paradigm of *A. africanus* and included in that of *A. robustus*, the specimen's place as the holotype of *A. africanus* would have to be revised. In any event, since the nominal species, *A. africanus*, was based on an immature stage lacking, to a certain extent, good diagnostic characters, the designation of a lectotype under Article 74 of the International Code of Zoological Nomenclature would seem desirable. The inclusion of the Taung skull in *A. robustus* would not automatically lead to its designation as the type specimen of this species: its juvenile status would probably preclude it from being so designated and the holotype of *A. robustus* would remain the skull, teeth and postcranial bones of the adult specimen, TM 1517, from Kromdraai, Transvaal.

I thank Dr V. J. Maglio for allowing me to quote from his unpublished manuscript, and also Dr T. C. Partridge, Professor K. W. Butzer, Mrs Kay Copley, Mr P. Faugust, Mr A. R. Hughes, Miss C. J. Orkin and Miss J. Walker. This work was supported by the Council for Scientific and Industrial Research (Pretoria), the University of the Witwatersrand (Bernard Price Institute), the Wenner-Gren Foundation for Anthropological Research and Educational Expeditions International (Boston).

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LETTERS TO NATURE

PHYSICAL SCIENCES

Ionospheric Effects of Cosmic γ -ray Bursts

THE recent discovery of bursts of γ rays of cosmic origin¹ has led to the suggestion that these bursts might produce observable ionospheric effects. Since γ rays are absorbed at a relatively low altitude when compared with most other types of ionising radiation, the thought was that these bursts would produce additional ionisation which might be strong enough to affect v.l.f. radio propagation data. If so and if data from several paths were obtained, it might be possible to obtain information about the location of the sources. Directional information from the Vela satellites, when obtained at all, contains an inherent ambiguity.

The calculations reported here were carried out by means of a Monte Carlo code which was developed to calculate X-ray and γ -ray transport in a model atmosphere. The model used is based on the 1962 COESA standard atmosphere². In the code it is described by 120 plane parallel layers, with each layer 1 km thick. Within each layer the density is assumed to decrease exponentially with altitude, and is described by a tabulated initial density and scale height for each zone. Above 120 km the atmosphere is assumed to provide negligible photon attenuation. The atmosphere is considered to have constant chemical composition, with photon cross sections as given by Storm and Israel³. Up to 120 km this approximation is quite good, but begins to become invalid at higher altitudes. Electron transport is neglected; that is, a photon which is absorbed or loses energy in a Compton collision is assumed to deposit all this energy in the 1 km zone in which the interaction occurs. This is a valid approximation, since at altitudes of from 20 to 40 km, the region in which most of the interactions take place, the thickness of the individual layers ranges from 9 g cm⁻² to 0.4 g cm⁻². The range⁴ of the highest energy Compton electron which can be produced is approximately 0.35 g cm⁻²; the vast majority of the electrons have considerably lower energy.

A calculation of energy deposition requires a knowledge of the incident spectrum. Spectral information from the Vela satellites is only qualitative, being based on total counts in two overlapping channels, with energy responses covering the

ranges from 0.2 to 1 MeV and 0.3 to 1.5 MeV, respectively. But since the original announcement of the Vela discovery, it has been learned that several of these events were also observed by the Goddard Space Flight Center γ -ray detector on board IMP-6 (ref. 5), and that one was seen by the two USCD X-ray telescopes on board OSO-7 (ref. 6). The IMP-6 and OSO-7 instruments provide overlapping spectral information for one event, 72-4 in the Vela catalogue, covering the energy range from 11 to 800 keV. This spectrum was used in the calculations reported here.

Several simplifying assumptions about the nature of the source were made in carrying out the calculations. The spectrum was assumed to be independent of time, although for most of the events observed by the IMP-6 detector the spectrum seems to soften somewhat with time. The time history as observed by both the Vela and OSO-7 satellites shows complex structure, but in the calculations it was assumed that the burst rose above background instantaneously and decayed exponentially, with a time constant of 20 s.

Table 1 Atmospheric Energy Deposition by Cosmic γ -ray Burst 72-4, having Total Incident Energy per Unit Area of 3×10^{-4} erg cm⁻²

Zenith angle (degrees)	Peak energy deposition (eV cm ⁻³)	Altitude of peak energy deposition (km)
0	85	28
6	86	29
12	85	29
18	82	29
24	76	29
30	72	29
36	66	30
48	49	31
60	33	32
72	16	33
84	3	40

Peak total energy deposition for various zenith angles is shown in Table 1. The ionisation is not very strongly dependent on zenith angle over quite a wide range. This particular event is not the strongest that has been observed in terms of total energy incident on the atmosphere, but it is not untypical. The peak energy deposition of approximately 85 eV cm⁻³ corresponds roughly to an electron production of 2 or 3

electrons cm^{-3} . It occurs at an altitude considerably lower than what is usually considered the lowest part of the daytime D layer. At that altitude the only competing process is ionisation by galactic cosmic rays⁷. In fact, at high geomagnetic latitudes the magnitudes of the two effects are comparable. This is shown in Fig. 1, where the steady state electron density produced by galactic cosmic rays at geomagnetic latitude greater than 70° is compared with the total number of electrons produced over a period of 80 s by γ -ray burst 72-4.

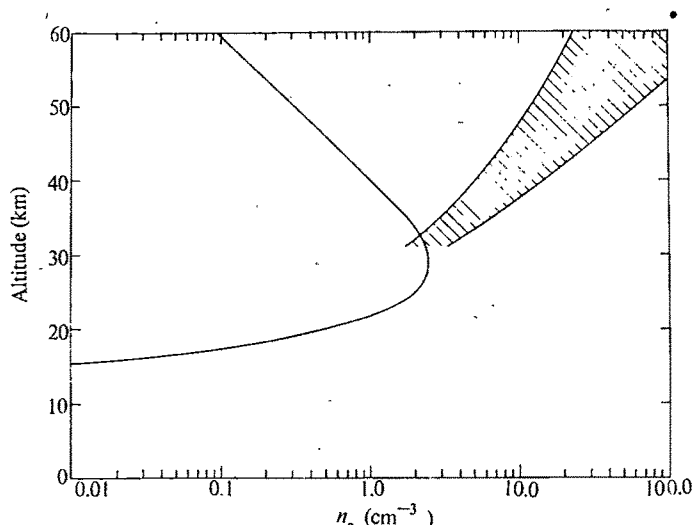


Fig. 1 Total electron density produced by cosmic γ -ray burst 72-4 compared with the steady state electron density produced by galactic cosmic rays. Cross-hatched area covers extremes of night-time solar maximum and day-time solar minimum as calculated by Webber⁷ for geomagnetic latitude greater than 70° .

So the best chance of observing these bursts would be at low geomagnetic latitudes, where the ionisation induced by galactic cosmic rays would be of a lesser magnitude than that produced by the burst. The burst would produce only a very transient effect, since at the altitudes at which the peak ionisation occurs the effective recombination coefficient is a very rapidly increasing function of decreasing altitude⁷. This requires that data be recorded on a finer time scale than is usually the case when, for example, the effects of geomagnetic activity are being studied⁸.

This work was performed under the auspices of the US Atomic Energy Commission. I thank I. B. Strong for suggesting this study, W. H. Tucker and T. J. Rosenberg for suggestions and T. L. Cline and M. P. Ulmer for furnishing data in advance of publication.

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Structure of the Terrestrial Planets

BULLEN¹ has suggested that to reconcile known data for Venus, Earth and Mars with the hypothesis that they have the same overall composition, the outer core of the Earth may be composed of Fe_2O . The principal reason seems to be the resolution of an alleged discrepancy between the modern solid radius of Venus determined by radar², $6,053.7 \pm 2.2$ km and the value of 6,270 km computed by Bullen on the phase-change hypothesis for the core³. But this latter value was arrived at on the basis of somewhat approximate calculations, whereas more accurate calculations⁴ find no discrepancy of any significance in interpreting Venus as possessed of three main zones with mechanical-elastic properties the same as in the corresponding zones of the Earth. In such calculations some allowance for the existence in Venus of a small inner core could readily be made, but it is clear that no adjustment for such an inner core, which in the Earth has volume only 0.76% of the whole, could seriously affect the computed value of the overall radius. For if the inner core were completely annihilated and the Earth contracted down geometrically without change of volume of the remainder, the outer radius would shrink only by 16 km, so that averaging of its properties with those of the main bulk of the core would produce negligible change of radius, whereas Bullen's discrepancy is over 200 km.

Although the possibility that the core consists of Fe_2O cannot be ruled out, there seems to be no need to postulate this, or any specific composition as to its chemical nature, when it comes to the question of calculation of the internal structures of other planets on the hypothesis that they have the same overall composition as the Earth itself; it is only the elastic constants and uncompressed density of the material that enter such calculations. Even if the properties of Fe_2O at pressures in excess of 10^{12} dyne cm^{-2} and temperatures of say 5,000 K ($\pm 2,000$ K) could be accurately calculated, its identification as core material could be based only on the agreement of its elastic constants and density with the known values derived for core material from the seismic data. Because these latter values are reliably known anyway for the Earth, they can be transferred immediately for use in regard to the other planets, without raising the question of absolute composition. When that is done the modern radar value for the solid radius of Venus leads to no difficulty in arriving at an acceptable internal structure. On the other hand, there could be no guarantee that other compounds may not have the same elastic properties and density as Fe_2O at the conditions concerned, and thus making detailed identification superfluous.

Adopting the round figure of 6,055 km for the radius, the model that is most plausible on the phase-change hypothesis has the following properties⁴: m_c =mass of core= 1.20×10^{27} g=0.247 mass of Venus; ρ_c =central density= 11.45 g cm^{-3} ; p_c =central pressure= 2.70×10^{12} dyne cm^{-2} ; r_c =radius of core=3,032 km=0.5008 radius of Venus; p_{12} =pressure at core/mantle boundary= 1.23×10^{12} dyne cm^{-2} ; r_m =radius to mantle/outer-shell boundary=5,540 km=0.915 R_V ; m_{12} =combined mass of core and mantle= 4.11×10^{27} g=0.844 M_V ; p_{23} =pressure at top of mantle= 0.16×10^{12} dyne cm^{-2} ; ρ_m =mean-density of whole planet to solid surface= 5.233 g cm^{-3} ; f =moment-of-inertia factor=0.3424; W =total (negative) gravitational energy= 0.1703×10^{40} erg.

If the pressure p_{12} at the core/mantle interface and the pressure p_{23} at the mantle/outer-shell interface were both assigned, then a unique surface radius r_s would result. Conversely, if the radius is regarded as known, then only one or other of these pressures is disposable. Where p_{23} is concerned, there is experimental evidence⁵ that the phase change involved is influenced by the temperature in the sense that higher pressure is needed to bring it about at higher temperature. In the Earth, the value of p_{23} is at present about 0.14×10^{12} dyne cm^{-2} . Calculations for Venus have been made³ covering a range of values of p_{23} from 0.12 to 0.16 ($\times 10^{12}$ dyne cm^{-2}),

and these show that the pressure p_{12} at the boundary of the core ranges only from about 1.22 to 1.27 ($\times 10^{12}$ dyne cm^{-2}), whereas the pressure at the core boundary in the Earth is 1.37 ($\times 10^{12}$ dyne cm^{-2}). If this boundary is regarded as an abrupt change of composition, then no special inference could be drawn from these lower pressures for Venus, but if it represents a phase change to metallic-liquid form, then this change being such that its production at lower pressure requires higher temperature, the inference would be that Venus is at somewhat higher internal temperature than is the Earth at this boundary. This is consistent with heating through radioactivity requiring longer for the central temperature to rise to an adequate level before bringing on the sudden Ramsey collapse^{6,7}, with part of the vast gravitational energy thereby released further increasing the temperature. For these reasons, a higher temperature might well also be implied for the mantle/outershell boundary, and the value 0.15 ($\times 10^{12}$ dyne cm^{-2}) was therefore selected to accord with this in settling the above most likely model. Venus would reach this stage later than the Earth, and its whole internal development may be lagging behind that of the Earth by some fraction of an aeon. Higher internal temperature for Venus might also receive some contribution through its greater proximity to the Sun coupled with a long-sustained greenhouse effect.

The proportion by mass of Venus in its core is seen to be 24.7%, compared with 31.4% for the Earth, and with the radius fixed at 6,055 km no serious change of this percentage is possible for any reasonable adjustment of the interface pressures. (If the radius is taken to be larger, the percentage is reduced.) Indeed, if Venus were to have the terrestrial properties by mass in its core, the radius could not be greater than about 5,980 km—more than 70 km less than the observed value. On the hypothesis that the terrestrial planets and the Moon have similar compositions, homogeneous on a sufficiently large scale, so that the known elastic constants and uncompressed densities for the various zones of the Earth can be utilized to compute models of these bodies, then the following scheme of possible explanation of their structures, as regards the presence or otherwise of a core, emerges from the presently known values of their masses and radii (Table 1).

Table 1 Properties of Terrestrial Planets

	Mass	Mean density	Percentage mass in core	Possible explanation
Earth	1.0	5.52	31.4	Iron or phase change
Venus	0.815	5.23	24.7	Iron or phase change
Mars	0.108	3.92	0.0	No metallic core
Mercury	0.055?	5.42?	60.0	Iron core only
Moon	0.012	3.35	0.0	No metallic core

For the purpose of computing the percentages of Table 1, no discrimination need be made between the time-honoured iron hypothesis and the Ramsey phase-change hypothesis for the terrestrial core, because the parameters needed depend solely on the seismic data for the Earth. On the first hypothesis, comparing the core masses with that of the Earth, each of the other bodies is seen from Table 1 to present a problem in varying degree. It would be necessary to suppose that Venus had distinctly smaller proportion of iron than the Earth, whereas the slightly more distant Mars and the closely adjacent Moon, without iron cores at all, would have considerably less proportion of iron overall and the present mass and radius of Mercury would require this planet to be a most remarkable object with about 60% of its mass in the form of an iron core and its whole iron content presumably greater still. On the phase-change hypothesis, however, these striking differences between the bodies follow immediately as a direct consequence of the internal pressures resulting from the differences in mass, the only difficulty being the egregious Mercury.

The value for the mean density of Mercury depends not only on that found for the mass but, even more sensitively, on that for the radius. Modern determinations, which are made by a combination of radar measures and dynamical theory, may nevertheless be influenced from the outset through the adoption, as starting values for linearized correction, of the mass originally announced by Rabe⁸ in 1950 from the orbit of Eros, and of the optically observed radius. Just as, to take a simple example, Newton's method may fail to find the appropriate root of an equation if the starting value selected happens to lie too close to another inapplicable root, so in the present case the situation may be such that arrival at the correct mass may automatically be prevented. This 1950 value for the mass has recently been practically withdrawn as to its reliability by Rabe⁹, who on further investigation of the method finds the (reciprocal) mass in fact to be subject to a probable error in excess of 50%. The difficulty of determining the radius of a small object lying so close to the Sun is of course so generally appreciated as to call for no further comment here.

The importance of the forthcoming Venus-Mercury flyby for resolving the seemingly anomalous structure of Mercury is self evident. Until confirmation by such means is available it seems scarcely worthwhile endeavouring to explain how it may have come about, or further still how the apparently strange composition may affect theories of the origin of the planets. On the basis of the phase-change hypothesis, a mean density for Mercury less than that of Mars would seem a reasonable expectation.

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PROFESSOR BULLEN replies: The statement¹ that "The principal reason for [the Fe₂O proposal] seems to be the resolution of an alleged discrepancy between the modern solid radius [R_v , say] of Venus determined by radar . . . and the value computed by Bullen on the phase-change hypothesis" does not put the facts in correct perspective.

I gave² four independent objections to the phase-transition theory, the discrepancy over R_v being only one item. More potent objections³ are: (a) the difficulty of reconciling the phase-transition theory with the large density jump at the Earth's mantle core boundary; (b) the failure to obtain support for that theory from shockwave high-pressure experiments. These objections have caused perhaps a majority of geophysicists to "rule out" the theory. My estimate is that the above objections make it desirable to explore alternatives, of which the Fe₂O theory is one. That theory, in contrast to the phase-transition theory, has the special strength that it avoids the potent objections ((a) and (b)) while yielding fair agreement with the relevant observational data. Lyttleton¹ disregards this vital point.

I do not agree that my 1950 estimate³ of 6,270 km for R_v , which assumed the phase-transition theory, is less dependable than Lyttleton's later calculations^{4,5}. I regard the opposite as the case. My calculations used numerical integration along with direct numerical detail on the Earth's density and pressure

distributions, and the procedures were formally reliable within ~ 10 km for R_V . In contrast, Lyttleton's calculations introduced a number of implicit assumptions which I did not find necessary and which distorted the starting Earth model, making his numerical results distinctly less reliable than mine (see also ref. 6).

Further, Lyttleton shows a lack of grasp of what the Fe_2O theory does in respect of planetary core radii. He refers to the volume of the Earth's inner core being only 0.76% of the volume of the Earth and infers that the presence or absence of an inner core in Venus would therefore have negligible effect on the estimated R_V . What is not appreciated is that the very large reduction of order 200 km from my estimate of R_V on the phase-transition theory to that on my Fe_2O theory arose principally because the Fe_2O theory entails relatively larger inner cores in smaller planets; for Venus, the inner core is given as not merely relatively larger than in the Earth, but actually as having nearly six times the volume of the Earth's inner core. On the Fe_2O theory, the Venus inner core has 4.4% of the volume of Venus. A consequence is that the change in the estimated R_V on the two theories is by no means negligible.

Why then does the Venus model detailed in ref. 1 have a value so close to the present observed value of $\sim 6,050$ km. I attribute this partly to some of the unreliable features of Lyttleton's procedures (see ref. 6), partly to *ad hoc* assumptions made by Lyttleton, and partly to his provision for possible temperature differences; this provision places an additional parameter at his disposal in a way that amounts to a further *ad hoc* device.

A very important corollary to the substantially larger inner core for Venus entailed on the Fe_2O theory is that the outer core of Venus is small compared with the Earth's outer core. Thus (assuming the dynamo theory of planetary magnetic fields), the Fe_2O theory fits better than all other theories the failure to detect a magnetic field around Venus.

While conceding that my Fe_2O theory cannot be "ruled out", Lyttleton questions the need for postulating any specific composition in planetary interiors. I have already indicated that one important reason for proposing the Fe_2O theory is that it avoids the objections (a) and (b). Moreover, a key property of Fe_2O for present purposes is essentially physical—the instability assumed at pressures less than a critical pressure (which corresponds to that at the Earth's mantle-core boundary). It is conceivable that the Earth's outer core could be composed of another material which exhibits this instability; if such a material should be found there could be a case for its investigation in respect of planetary structure.

More serious, however, is the statement¹ that the "identification [of Fe_2O] as core-material could be based only on the agreement of its . . . density with the known values derived . . . from seismic data". No reference is made to Soroktin's calculations that Fe_2O has the assumed instability and that its density-pressure relation for conditions prevailing in the Earth's outer core matches that in recent Earth models (see, for example, ref. 8).

Lyttleton's comment on the considerable uncertainty of the observational mean density of Mercury is interesting. Because of the uncertainties it has seemed to me that all that can, on present evidence, be reasonably said on the internal structure of Mercury was said by 1952. It has long been established that "on the basis of the phase change hypothesis a mean density for Mercury less than that of Mars would appear to be a reasonable expectation" (see, for example, ref. 9).

No useful favourable test of Lyttleton's theory has emerged since it was promulgated some ten years ago, but there are² possible tests of the Fe_2O theory in the foreseeable future. I seem to differ from Lyttleton in that I do not wish to press any particular theory beyond what I regard as the balance of evidence. Should future tests favour the phase-transition theory, no one would be more delighted than myself because of my earlier association with it. But it seems to me that,

on a proper weighting of current evidence, including points (a) and (b) above, the Fe_2O theory has fewer difficulties to meet than the phase-transition theory.

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Refining the Earth's Pear Shape

QUITE soon after the launching of the first artificial satellites, analysis of their orbits led to the reshaping of the world. The orbital plane of Sputnik 2 rotated less rapidly than expected, indicating¹ that the polar flattening was about 0.35% less (the polar diameter about 150 m greater) than had been thought. The variations in the perigee height of Vanguard 1, as perigee moved successfully north and south of the equator, showed² that the polar section of the geoid—the profile of the sealevel surface revealed by a cut through the poles—was not symmetrical about the equator but had a slight pear-shape tendency, with the stem at the North Pole. Floating at sealevel at the North Pole, one would be about 40 m further from the equator than an equally undaunted explorer who bored down to sealevel at the South Pole.

Since 1959 the odd zonal harmonics in the geopotential, which determine the extent of the pear shape, have been evaluated with improving accuracy and reliability, from analysis of satellite orbits at a wide variety of inclinations to the equator. But until recently no suitable satellites have been available with near-equatorial orbits or with orbits close to the critical inclination of 63.4° , where the perturbations caused by the odd harmonics become extremely large, 50 km or more. In this letter we report the results of a new determination of the odd zonal harmonics³ from the orbits of twenty-seven satellites, including two orbits close to the critical inclination, determined with the help of observations from the Hewitt cameras at Malvern and Edinburgh.

If variations with longitude are ignored, the geopotential U at an exterior point distant r from the Earth's centre and having geocentric latitude ϕ , may be expressed in the standard form¹

$$U = \mu/r \left\{ 1 - \sum_{n=2}^{\infty} J_n (R_e)^n P_n (\sin \phi) \right\} \quad (1)$$

where μ is the gravitational constant for the Earth ($398,601 \text{ km}^3 \text{ s}^{-2}$), R is the equatorial radius ($6,378.14 \text{ km}$) and $P_n (\sin \phi)$ is the Legendre polynomial of degree n and argument $\sin \phi$. The coefficients J_n are to be determined.

The variations of gravity with longitude, although ignored in equation (1), can be measured, and the variations of the geopotential with both latitude and longitude, in terms of tesseral harmonics, have been evaluated by analysing observations of satellites with cameras and lasers, and also by Doppler radio tracking, combined with ground-based data such as gravimetric measurements. Two recent examples are the Smithsonian Standard Earth III (ref. 4) and the Goddard Earth Model 4 (ref. 5). The neglect of the longitudinal variations in equation (1) means that U represents

a longitude-averaged potential, and therefore gives a longitude-averaged polar section of the geoid.

The even zonal harmonics, with coefficients $J_2, J_4, J_6 \dots$ are symmetrical about the equator; the odd zonal harmonics, with coefficients $J_3, J_5, J_7 \dots$ are antisymmetrical about the equator. The dots in the previous sentence nicely express the crux of the problem of determining the coefficients: how do you evaluate an infinite set of coefficients from finite data? In practice, the usual method is to analyse the orbital variations in as many satellites as possible, having the most varied available orbits, and to evaluate the coefficients by truncating the series of harmonics when the inclusion of further coefficients seems to bring no advantage.

Table 1 Values of Eight Coefficients

$10^9 J_3 = -2,531 \pm 7$	$10^9 J_{11} = 159 \pm 16$
$10^9 J_5 = -246 \pm 9$	$10^9 J_{13} = -131 \pm 22$
$10^9 J_7 = -326 \pm 11$	$10^9 J_{15} = -26 \pm 24$
$10^9 J_9 = -94 \pm 12$	$10^9 J_{17} = -258 \pm 19$

Our recent determination of the odd zonal harmonics⁸ utilised twenty-seven orbits, at inclinations to the equator ranging between 3° and polar, and we found the most satisfactory least-squares fit to the data was obtained by evaluating eight coefficients, J_3 to J_{17} . Their values are given in Table 1.

The values are determined by fitting the nearly sinusoidal variation in perigee height experienced by the twenty-seven satellites, and the effect of the complete set of harmonics is best characterised by the amplitude β of the oscillation in eccentricity which they produce in a standardised orbit. Figure 1 shows the values of β for an orbit with near-zero eccentricity and semi-major axis $a=7,087$ km ($=R/0.9$).

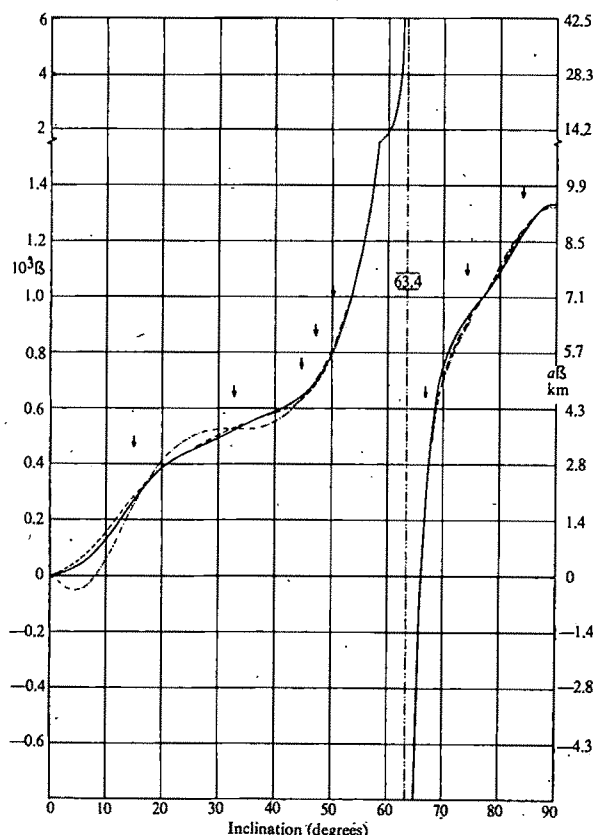


Fig. 1 Variation of β with inclination for $R/a=0.9$ and $e=0$, given by our solution (—), Wagner's⁶ (---) and Kozai's⁷ (-·-·-). Arrows indicate the inclinations of satellites in all three.

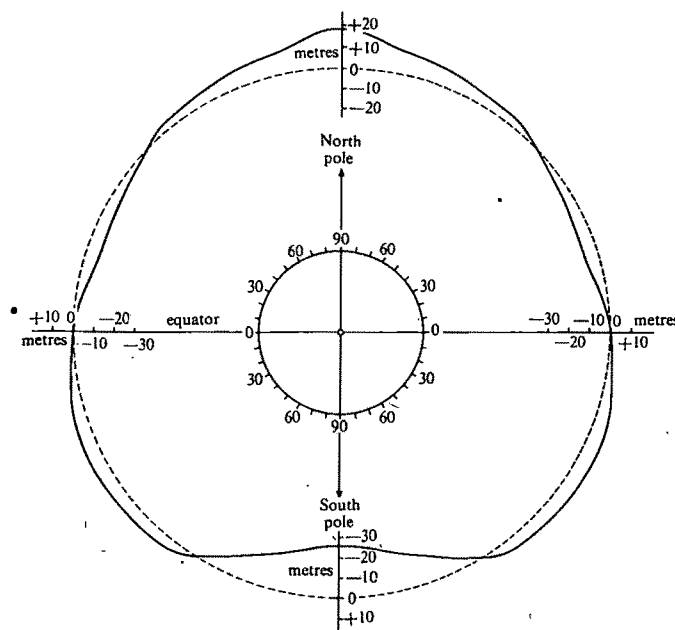


Fig. 2 Height of the meridional geoid section (—) relative to a spheroid of flattening 1/298.25 (---). (With our odd harmonics and Wagner's⁶ even harmonics.)

Figure 1 also indicates the amplitude of the oscillation in perigee height, $a\beta$, which is nearly independent of a . The diagram gives the value of β for our set of odd zonal harmonics (solid line); for that obtained from twenty-one orbits by Wagner⁶ (broken line); and for that obtained from fourteen orbits by Kozai⁷ (dot-dash line). Our predicted values of $a\beta$ agree with Wagner's to within 200 m except very close to 63.4°, but Kozai's values tend to oscillate about ours, and differ by up to 700 m at some inclinations. There are eight satellites common to all three of these determinations of the odd harmonics, and it is noticeable that the values of β agree well at the inclinations of these satellites, indicated by arrows in Fig. 1. Much of the difference between the three sets no doubt arises from the different individual coefficients evaluated: we chose J_3 to J_{17} ; Wagner chose J_3 to J_{21} ; and Kozai chose J_3 to J_{23} plus J_{35} .

Our previous set of odd zonal harmonics⁸ indicated that the pear-shape tendency of the Earth—the north polar radius minus the south polar radius—amounted to 40 m. The new set of values gives a geoid which is the same to within 1 m over most of the latitude range, but shows larger differences (of up to 2.3 m) at latitudes of 88° to 90°, with the north pole quite literally 'growing a stem', like a pear. Consequently the pear-shape tendency, as defined above, is now greater, 44.7 m instead of 40 m. In presenting a profile of the geoid, it is also necessary to choose a set of even zonal harmonics, and Fig. 2 shows the geoid profile (solid line) relative to a spheroid of flattening 1/298.25 (broken line) with our set of odd zonal harmonics and Wagner's set of even zonal harmonics⁶. (The use of Kozai's even harmonics⁷ does not alter the profile by more than 0.3 m.) Figure 2 shows that the north polar stem of the pear may be taken as 18.9 m high, whereas the south polar depression is 25.8 m below the spheroid. Since the change from the 1969 values amounted to less than 1 m over most of the latitude range, the profile in Fig. 2 should be accurate to 1 m, although of course it represents an average over all longitudes rather than a specific physical profile.

In conclusion we emphasise that, in spite of the good accuracy of the geoid section, there is still much room for improvement in evaluating the odd zonal harmonics. There are gaps in the coverage in inclination at angles between 6° and 14°, between 16° and 28° and between 33° and 41°. Until these gaps are filled by the launch of suitable satellites,

the validity of the fitting of β in the empty regions will remain open to question.

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Microearthquake Study of the Mid-Atlantic Ridge near 37° N, using Sonobuoys

IN view of the successful use of telemetering radio sonobuoys for detecting and locating microearthquakes in the Gulf of California¹, we carried out a similar survey of the Mid-Atlantic Ridge, in the region near latitude 37° N, during May and June of this year. Our object was to study the level of distribution of seismicity; in particular, we hoped to locate some earthquakes sufficiently accurately that we could associate them with local physiographic features, and draw conclusions about the present tectonic activity of this section of the ridge. Teleseismic study of the mid-ocean ridge suffers from two basic limitations: the epicentral locations are not sufficiently accurate to allow more than a general correlation of seismic activity with the median rift (where present) and with the transform faults offsetting the ridge segments², and it is not generally possible to locate earthquakes of magnitude less than about 4 (ref. 3). Ocean

bottom seismometers have also been used to study ridge seismicity, but the results to date have been fairly limited.

The study described here was undertaken as an ancillary programme on cruise 31 (WHOI TOW I) or RV Knorr (Woods Hole Oceanographic Institution). The main object of this cruise was a detailed survey of the area, using the Scripps Institution of Oceanography/Marine Physical Laboratory's deep-tow instrument package⁵. This, in turn, was part of a continuing intensive study of this section of the Mid-Atlantic Ridge (Project FAMOUS). As a result, the topography is well enough known to allow meaningful correlation with the seismicity.

The technique used was basically that described by Reid *et al.*¹ for the Gulf of California. Expendable sonobuoys⁶ were monitored by onboard recording equipment. The sonobuoy positions were found by firing explosive charges to determine their range from the ship. Whenever possible, we tried to maintain an array of at least three sonobuoys operating, with a spacing of a few kilometres. We obtained fifty-nine epicentral locations, out of 104 earthquakes recorded during 11 d of favourable recording conditions. More than half the locations have an estimated error of 2 km or less.

Figure 1 shows the record of a typical event at a distance of about 30 km. We follow the phase identification and nomenclature of Reid *et al.*¹. The P and S arrivals are the direct compressional and shear waves through the crust, and the T phase is interpreted as the wave travelling through the water layer from the epicentre. At distances less than about 10 km, S and T phases are not normally seen, and the observed phases are P and its reflections in the water column, designated P₁, P₂, and so on.

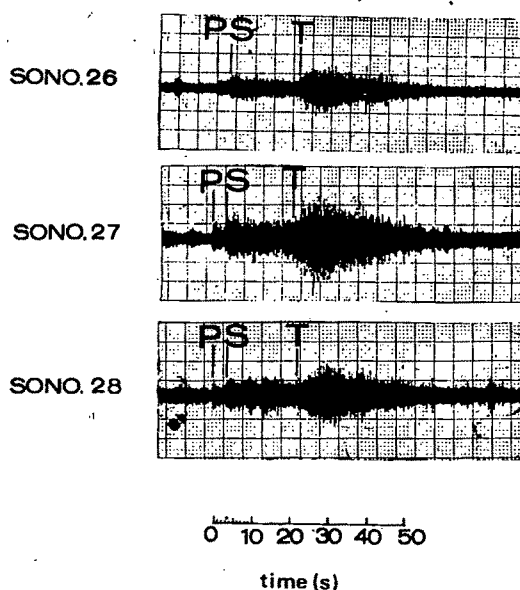


Fig. 1 Recording of a typical earthquake detected on sonobuoys. The epicentral distance is about 30 km. (This is not the original record but a replay off magnetic tape.)

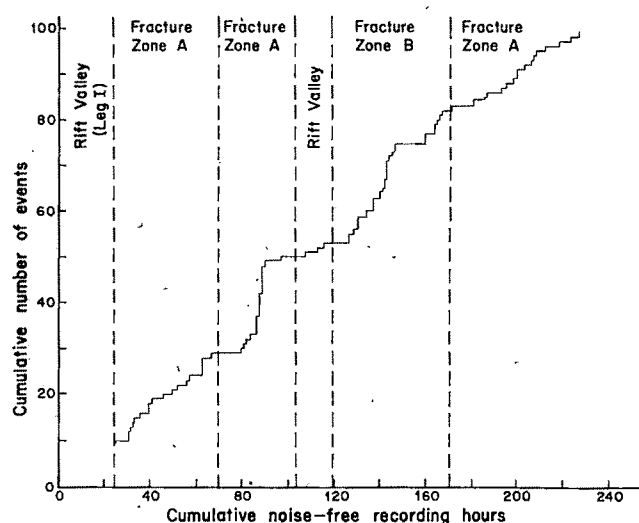


Fig. 2 Cumulative number of earthquakes recorded against cumulative number of low-noise recording hours. The dashed vertical lines indicate the successive sonobuoy arrays.

The results are summarised in Figs 2 and 3. Figure 2 is a plot of cumulative number of earthquakes recorded against cumulative number of low-noise recording hours, and Fig. 3 shows the located epicentres superposed on a bathymetric contour map of the area. As Fig. 3 shows, the study area includes a ridge segment with a well defined median rift, 45 km long and averaging 7 km width. This is terminated by two fracture zones, designated fracture zone A (to the north) and fracture zone B (to the south), which offset the ridge from its continuations. Figure 2 also shows in which part of the area the sonobuoy arrays were placed. On the first leg of the cruise, during which the main survey of the rift took place, the weather was consistently poor, result-

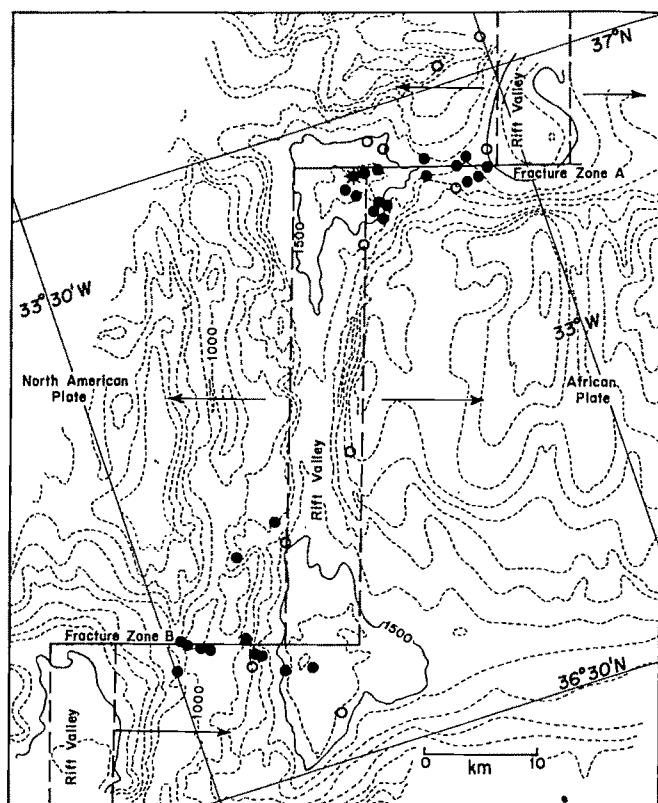


Fig. 3 Map of the best located epicentres, superposed on a bathymetric map of the area. The tectonic interpretation shown is a simplified approximation. ●, Good locations (generally with less than 2 km error); ○, less reliable locations (up to about 5 km error). The star-like symbol at the west end of fracture zone A represents a swarm-type sequence of about seven recorded events.

ing in a noise level too high for effective recording. During the second leg, operations were concentrated on the fracture zones, particularly fracture zone A, and this is reflected in Fig. 2 and in the density of epicentres in Fig. 3.

The seismicity seems to be quite uniform in time (Fig. 2) and the same for both fracture zones. The sample of rift seismicity is not sufficient to allow firm conclusions to be drawn, but it seems lower than the fracture zone seismicity. Figure 2 has been compiled from the raw data, with no corrections for earthquake magnitude or for distance from the array. But we believe Fig. 2 is a fair representation of the seismicity, at least for the fracture zones. We have not attempted any individual magnitude estimates; the detection threshold for a nearby event is about $M=0$, and we estimate most of the earthquakes recorded to be between $M=0$ and $M=1$. In contrast to the Gulf of California or the Galapagos spreading centre, where microearthquake swarms seem to predominate^{1,7} there were only two or three swarm-like sequences⁸ recorded, consisting of up to seven closely spaced events. The microseismicity, at ten events per day, is comparable with that on active sections of the San Andreas Fault⁹, and is consistent with the number of teleseismically detected earthquakes occurring along this section of the Mid-Atlantic Ridge¹⁰.

Figure 3 demonstrates the excellent correlation of the seismicity with the fracture zones deduced from the topography. It clearly shows that most activity is restricted to the section of fracture zone between the rift segments, that is the section where transform faulting¹¹ is occurring. Along fracture zone B, the seismicity appears to delineate a simple transform fault, characterized by a narrow line of epicentres and narrow topographic notch (seen on the deep-tow data but not on the Fig. 3 map). Fracture zone A comprises a

broader region of deformation, with a number of fault scarps and grabens (R. Detrick, personal communication). Most of the computed fracture zone A epicentres, however, lie within 1 km of a straight line, well inside the location uncertainty, which we estimate to be less than 2 km in most cases. This suggests that only one fault plane may be presently active. The active transform faults, as delineated by the seismicity, seem to be narrow and linear, even on a small scale. They are also active over their entire length, even over short time intervals. They show the usual orthogonality to the ridge axis¹².

The junctions of the fracture zones with the median rift are characterized by topographic depressions. The deep-tow study showed that the depression at the junction of fracture zone A with the central rift is bounded on the north by a well defined fault scarp, which we interpret as the active transform fault. This scarp showed a high level of seismic activity, including the only located swarm, and we located one event on this scarp with particularly high accuracy (within 0.5 km). This suggests that active transform faulting continues well into the central rift valley, and hence, that the spreading centre plate boundary (or zone of intrusion), is itself a narrow feature within the central valley.

Because of the small sampling and, we believe, lower seismicity, there are hardly any reliable locations along the rift itself. Such evidence as there is suggests that the seismicity may be concentrated near the edge of the rift, and that there is essentially no activity outside the rift. This would be expected if normal faulting on the rift walls were the dominant source of rift earthquakes¹³. If the low microseismicity of the rift, particularly the low incidence of swarms, is real, then this is in sharp contrast to the Gulf of California and the Galapagos spreading centre, where the spreading segments are highly active^{1,7}. This might indicate less volcanic activity on this slower spreading ridge⁸.

We found it difficult to obtain accurate focal depths in this study, due to array limitations. In one case we found a focal depth of about 1 ± 1 km for a fracture zone A event. Other evidence, particularly the predominant T phase of many events, suggests an equally shallow source for most of the events recorded. In obtaining the epicentre locations, we have generally assumed zero focal depth and a P velocity of 5 km s^{-1} . This should not lead to appreciable errors in most cases. In general, the detailed seismicity and earthquake distribution seem to be in good agreement with current ideas on mid-ocean ridge plate tectonics.

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Location of Hydrogen Atoms in ADP by Neutron Powder Profile Refinement

NEUTRON diffraction is a powerful tool for the location of light atoms, especially hydrogen, because the neutron scattering power of these atoms is comparable to that of the heavier elements. In particular, the study of hydrogen bonding and its effect on the physical properties of molecular crystals is well suited to neutron diffraction techniques. Unfortunately, because of the relatively low flux of thermal neutrons available, even from the best reactors, rather large single crystals are required, together with expensively long periods of time for data collection. Even when large crystals can be grown, multiple scattering (extinction effects) introduce systematic errors which limit the precision with which atoms can be located. It would be important then, if some way could be found to eliminate the need for large single crystals and long periods for data collection.

The powder diffraction method solves some of these problems, but it is usually thought that neutron powder patterns contain too little information to allow the solution of any but the most simple crystal structures. I argue that provided we abandon the traditional method of structure refinement

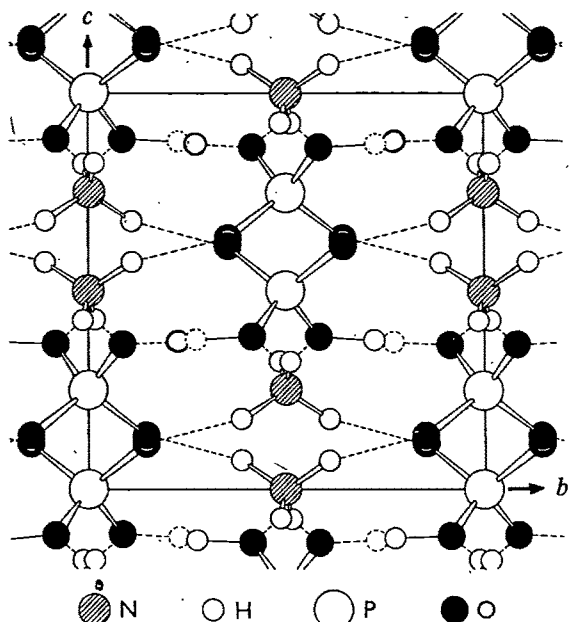


Fig. 1 The [100] projection of the $\text{NH}_4\text{H}_2\text{PO}_4$ structure showing the two positions between which the hydrogen atom linking PO_4 groups can tunnel (after Tenzer *et al.*⁴).

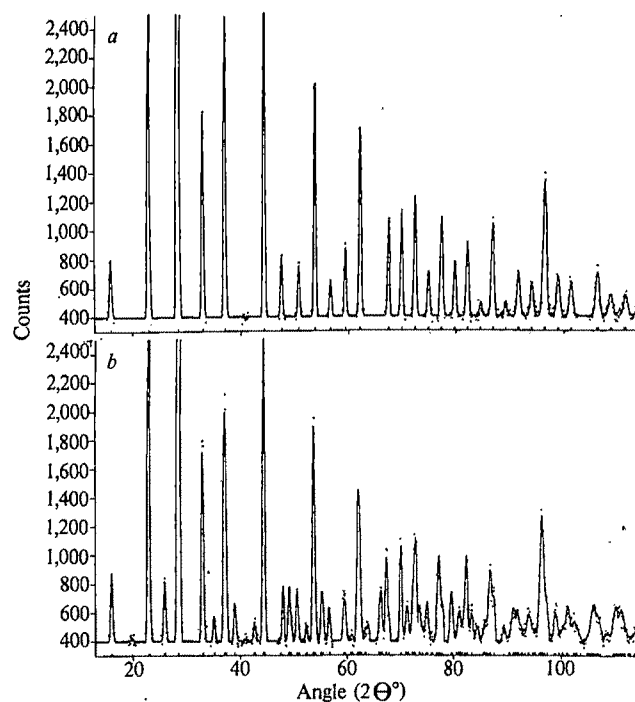


Fig. 2 Observed and calculated powder profiles of deuterated ADP for 1.54 Å neutrons. The positions of the separate Bragg reflexions contributing to these profiles, which were obtained in 22 h on the PANDA diffractometer at Harwell, are marked along the 2θ scattering angle axis. The superlattice lines in the low temperature phase appear because the ordering of the O-H . . . O hydrogen atoms reduces the symmetry from $I4_2d$ at room temperature (a) to $P2_12_12_1$ at 77.4 K (b).

based on the measurement of structure factors, there is much more useful information in a neutron powder pattern than is immediately obvious.

Information is lost, of course, because the crystalline grains in a powder have all orientations; the intensity scattered into a particular direction is the sum of all reflexions having that particular Bragg angle. Because of the finite resolution of a diffractometer, this usually results in a very complicated diffraction pattern from which it is impossible to resolve individual reflexions and to obtain a set of structure factors. Rietveld¹ has shown that in this case it is best to refine the structure to fit directly the observed diffraction pattern, rather than to try to extract the structure factors as an intermediate step. Fortunately, because of the simple radiation spectrum and geometry of a neutron diffractometer, the shape of a single Bragg powder peak is known very precisely for every scattering angle: it is a Gaussian. The positions of all these peaks are fixed by the crystal lattice constants, and so the detailed shape of the entire pattern must be determined solely by the positions of the atom in the crystal lattice; these positions can be refined to obtain the best agreement between the calculated and observed diffraction pattern "profiles".

This profile refinement technique has proved very valuable for the structure refinement of inorganic materials^{1,2}, but now I apply it to more complicated crystals, especially to hydrogen bonded structures. ADP, ammonium dihydrogen phosphate ($\text{NH}_4\text{H}_2\text{PO}_4$) is a rather single example, but the hydrogen bonds are responsible for a very interesting structural transition which occurs at ~ 245 K in the deuterated material. The (H_2) hydrogen atoms have two stable positions, close to one or the other of two oxygen atoms in adjacent PO_4 groups⁴. At room temperature these hydrogen atoms have sufficient energy to tunnel between the two stable positions, and the average occupancy of both positions is $\frac{1}{2}$. When the temperature is lowered the hydrogen atoms are presumably caught in one or the other of these positions, but there is no random

Table 1 Fractional Coordinates of the Deuterium Atoms on the O-H...O Bonds, obtained in this Experiment

	Paraelectric phase $I\bar{4}2d$				Antiferroelectric phase $P2_12_12_1$			
	$a=b=7.502 \text{ \AA}$ $T=22^\circ \text{C}$		$c=7.520 (2) \text{ \AA}^*$ $R=2.8\%$	Occupation	$a=7.507 \text{ \AA}$ $T=77.4 \text{ K}$	$b=7.529 (2) \text{ \AA}^*$	$c=7.445 (2) \text{ \AA}^*$ $R=2.8\%$	Occupation
	<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>	
D1	0.277 (3)	0.144 (1)	0.140 (4)	$\frac{1}{2}$	0.275 (3)	0.144 (3)	0.134 (3)	1
D2	0.223	0.144	0.110	$\frac{1}{2}$				0
D3	-0.144	0.277	-0.140	$\frac{1}{2}$	-0.146 (3)	0.277 (3)	-0.145 (3)	1
D4	-0.144	0.223	-0.110	$\frac{1}{2}$				0

* From observed ratios b/a , c/a : the neutron wavelength $\lambda=1.53 \text{ \AA}$ was not measured precisely.

In the low temperature antiferroelectric phase, these atoms are ordered on one of the two sites over which they are distributed in the room temperature paraelectric phase (see Fig. 3). The R factors are for separated structure factors, and the numbers in parentheses are the standard deviations for the parameters¹.

distribution; there seems to be an ordering of these hydrogen bonds which results in a distortion of the structure from tetragonal ($I\bar{4}2d$) to orthorhombic $P2_12_12_1$. This mechanism is similar to that found by Bacon and Pease³ to be responsible for the ferroelectric transition in KH_2PO_4 , but in the ammonium salt the transition is antiferroelectric. It is important to find the reason for this difference, but experiments on the low temperature structure of $\text{NH}_4\text{H}_2\text{PO}_4$ are difficult: the crystal shatters when passed through the transition because the different domains distort in different directions. This difficulty has held up the solution of the low temperature structure for twenty years.

This experimental problem does not exist for a powdered specimen. In Fig. 2 I show the diffraction pattern obtained in 22 h from 15 g of deuterated ADP, both above (a) and below (b) the transition temperature. The strong "super lattice" reflexions observed in the low temperature phase reflect the lowering of the symmetry which occurs when the deuterium atoms order on one or the other of the sites available to them, thereby distorting the whole structure. The solid lines in these diagrams represent the calculated profiles which best fit the observed points. In both cases, the fit approaches that expected for purely statistical errors in the count. The coordinates and vibrational amplitudes of all of the atoms in both structures have been obtained, but the structural transition can most simply be described if I refer only to the (H_2) hydrogen positions.

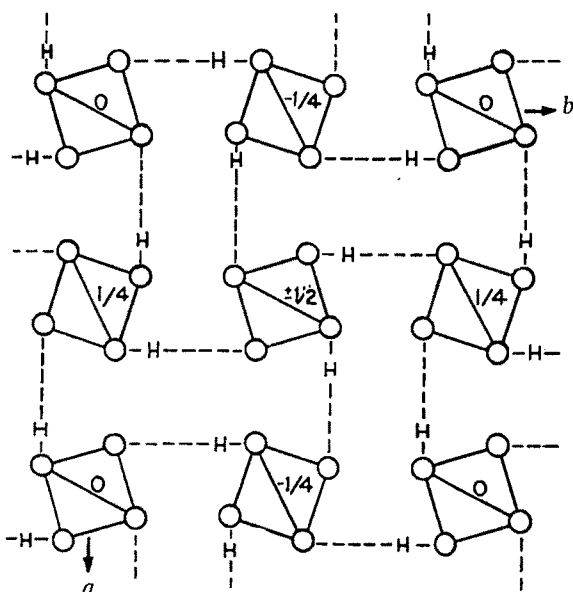


Fig. 3 Ordering of the deuterium atoms (H) on the hydrogen bonds between the phosphate groups, as proposed by Nagamiya⁵ and verified in the present experiment.

In Table 1 I give the coordinates obtained for the two equivalent hydrogen sites in the high temperature phase, when each is occupied for half of the time. In the low temperature phase, I find that the diffraction pattern can be explained if I assume that only one of these alternative positions is occupied. When the occupation numbers for the two positions were refined, starting with $\frac{1}{2}$ for both, the one approached unity while the other approached zero within the limits of uncertainty imposed by the data (1.0 ± 0.1). Figure 3 shows how these positions are taken up to produce a perfectly ordered arrangement of hydrogen bonds, but one in which there is no net dipole moment for the complete cell. This result confirms the ordering proposed by Nagamiya⁵. The PO_4 group at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$, which was equivalent to that at (000) in the high temperature phase, becomes inequivalent in the low temperature phase because of this ordering of hydrogen atoms. These phosphate groups, and the ammonium groups too, are slightly distorted by this hydrogen atom ordering (the ammonium groups are displaced as well), but the resulting dipole moments cancel out over the entire cell and the low temperature structure is antiferroelectric rather than ferroelectric as in KH_2PO_4 .

Finally I note that the profile powder method is a technique for structure refinement: it is not intended to compete with methods such as those based on Fourier techniques for the solution of structures about which very little is known. But with neutron diffraction we are almost always trying to refine the details of a structure which has already been solved approximately by X-ray or other techniques—finding more precise positions for the atoms, especially those of hydrogen and the lighter elements, measuring magnetic moments, nuclear and magnetic disorder, defect structures, atomic vibrational amplitudes and so on. For these structure refinement problems the profile refinement of neutron powder patterns often has many advantages over single crystal method. New designs for neutron powder diffractometers, giving greatly increased resolution and intensity, will allow larger structures to be studied with this technique.

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BIOLOGICAL SCIENCES

Suppression of Mouse Antibody Producing Spleen Cells by Various Interferon Preparations

POLYRIBOINOSINIC acid: polyribocytidylic acid [poly (rI)-poly (rC)], endotoxin, polycarboxylate plastics or polysaccharides, and other polyanions induce interferon production (see reviews ref. 1 and 2). They also enhance antibody production^{3,4}, cell-mediated immunity⁵, and reticulo-endothelial activity^{4,6}. It is not yet clear whether or not any of these latter effects are mediated through the action of interferon.

Recently, mouse interferon preparations from several different sources have been shown to enhance phagocytic activity in peritoneal macrophages cultivated *in vitro*⁷. Also, many reports have shown antitumour activity in interferon preparations both *in vivo* and in cell culture (see review ref. 2).

Attempts have been made to measure the effects of interferon preparations on *in vivo* antibody production, but these studies demonstrated either no effect⁸ or variable effects, including modest stimulation or inhibition⁹. Large amounts of interferon are required to simulate *in vivo* the circulating interferon levels produced by inducers such as poly (rI)-poly (rC), and past work has been restricted to interferon levels considerably lower than those obtained with inducers. Our studies were conducted with potent interferons, and measured the effects of a variety of interferon preparations on the number of mouse spleen cells producing antibody to sheep red blood cells (SRBC) during primary immunization. Interferon was administered in several large doses over 3 h, giving a reasonable simulation of both the levels and the time course of circulating interferon following poly (rI)-poly (rC)-administration.

Four different interferon preparations, stimulated by Newcastle Disease virus (NDV), were used: (1) pressure dialysed L₉₂₉ cell supernatant, (2) pressure dialysed C243-3C cell¹⁰ supernatant, (3) mouse serum, and (4) L cell interferon which was purified by affinity chromatography using anti-mouse interferon antibody to a purity of 1.96×10^8 units mg⁻¹ protein¹¹.

When 100 µg of poly (rI)-poly (rC) was given either 2 d or 4 d before antigen, a two-fold increase in the number of antibody producing spleen cells assayed 6 d after antigen administration occurred (Table 1). To determine the amount of interferon necessary to successfully simulate the circulating interferon levels induced by poly (rI)-poly (rC), two different doses of interferon were administered, sera were taken at various times, and then the interferon titres compared to those achieved after intravenous (i.v.) administration of 100 µg of poly (rI)-poly (rC). In one case approximately 1.8×10^5 units of L₉₂₉ cell interferon were administered i.v. in four divided doses over a 4 h period, in the other, approximately 4.2×10^4 units were similarly given. As can be seen from the results plotted in Fig. 1, the larger dosage schedule resulted in serum interferon levels approximately equal to that achieved by poly (rI)-poly (rC) while the lower dosage level did not achieve adequate serum levels to simulate the interferon production of the dose of poly (rI)-poly (rC) necessary to simulate an increase in the number of antibody producing spleen cells.

When 1.8×10^5 units of L₉₂₉ cell interferon were thus given 2 d before antigen (SRBC), at a time when poly (rI)-poly (rC) caused a marked enhancement of the number of antibody producing spleen cells as assayed 6 d after antigen administration (Table 1), we were surprised to note a sharp depression in the number of antibody-producing spleen cells to 16% of that in uninjected control animals.

This experiment was repeated several times with different interferon preparations. As can be seen in Fig. 2 and Table 1, as the interferon titre increased, the degree of depression increased, giving a sigmoidally shaped dose response curve characteristic of the antiviral action of interferon. Doses of over 1×10^5 units of interferon gave marked depression (16% of control), while doses between 5×10^4 units and 1×10^5 units showed an intermediate degree of depression with a greater degree of variability. Doses of less than 5×10^4 units showed no measurable depression.

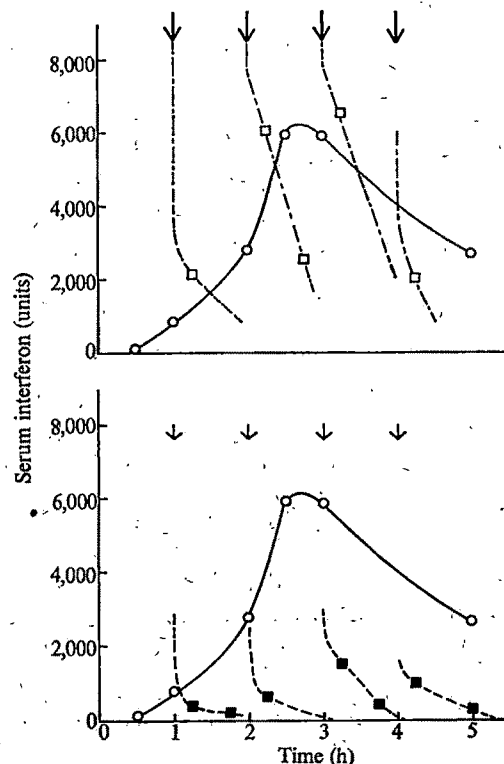


Fig. 1 Comparison of serum interferon attained after i.v. injection of various doses of interferon with that attained after induction by poly (rI)-poly (rC). Interferon titres were measured with a plaque reduction assay on mouse L₉₂₉-cell monolayers employing bovine vesicular stomatitis virus (VSV), Indiana strain, as a challenge virus²⁰. The interferon titre corresponded to the reciprocal of the highest dilution of sample which reduced virus plaque formation by 50%. Titration of the 6,000 unit mouse interferon standard distributed by the National Institutes of Health revealed a unitage of 2,490 units per vial in this assay. Serum levels of interferon attained in 6-week-old Swiss-Webster mice after intravenous administration of 100 µg of poly (rI)-poly (rC) at time 0 (○—○). Serum levels of interferon attained after intravenous administration of L₉₂₉ cell interferon (titre 5.2×10^4 units), 1.0 ml at 1, 2, and 3 h and 0.5 ml at 4 h (□—□), and after L₉₂₉ cell interferon (titre 1.2×10^4 units) at the same times and amounts (■—■). Clearance curves are extrapolated to expected concentrations at zero time after injection.

To test whether volume of injection or the presence of other non-interferon substances may be responsible for this effect, two preparations of supernatant from uninduced L₉₂₉ cell monolayers and one preparation of mouse serum from uninduced mice were inoculated in the same volumes as were the interferon preparations with no significant deviation from control values (Fig. 2). These preparations were in all respects processed and concentrated similarly to their corresponding interferon preparations, and all titred at less than 10 units of interferon. In addition, a portion of one batch of C243-3C cell interferon preparation was exposed to trypsin (0.25 mg ml⁻¹) for 1 h at 37° C and another heated to 56° C for 1 h. These preparations along with an untreated portion were inoculated into a series of mice. The untreated portion showed the usual immuno-

Table 1 Effect of Various Interferon Preparations on Antibody Producing Cells

Substances	Dose	Day of administration relative to antigen	Antibody producing cells* (% of mean control level)		No. of animals	Significance of difference from control
			Mean	Range of $\pm$ s.d.		
Poly (rI)·poly (rC)	100 μ g	2 d before	209%	175% to 251%	10	$P < 0.001$
Interferon, all types†	100 μ g	4 d before	170%	137% to 210%	7	$P < 0.05$
	$> 1 \times 10^5$ units	2 d before	16%	12% to 20%	9	$P < 0.001$
	4×10^4 units	†	76%	62% to 95%	8	$P < 0.11$
Affinity chromatography purified interferon	1.5×10^5 units	2 d before	19%	12% to 29%	2	$P < 0.001$
Human leukocyte interferon	1×10^5 units	2 d before	86%	56% to 131%	2	(NS)
C243-3C cell interferon						
Untreated	1.5×10^5 units	2 d before	17%	13% to 22%	3	$P < 0.001$
56° C for 1 h	2.5×10^4 units	2 d before	90%	62% to 132%	3	(NS)
Trypsin exposed§	$< 10^2$ units	2 d before	139%	84% to 233%	1	(NS)

* Statistical analysis of the results was carried out by linear regression analysis on the natural logarithms of the observed data, assuming orthogonality between any day-to-day variation in the baseline and experimental effects. The geometric (logarithmic) mean $\pm$ s.d. is given as a percentage of the mean control value. In the computer program used for this analysis, the reported s.d. and confidence limits of the experimental groups are expanded to include the s.d. of the mean control value. Duplicate assays were conducted on each spleen.

† Two animals received L_{929} cell interferon, six C243-3C cell interferon, and one mouse serum interferon.

‡ Five animals 2 d before, one animal 3 d before, and two animals 4 d before.

§ 25 mg ml⁻¹ for 1 h at 37° C.

|| Residual titre after treatment.

(NS) Not significant.

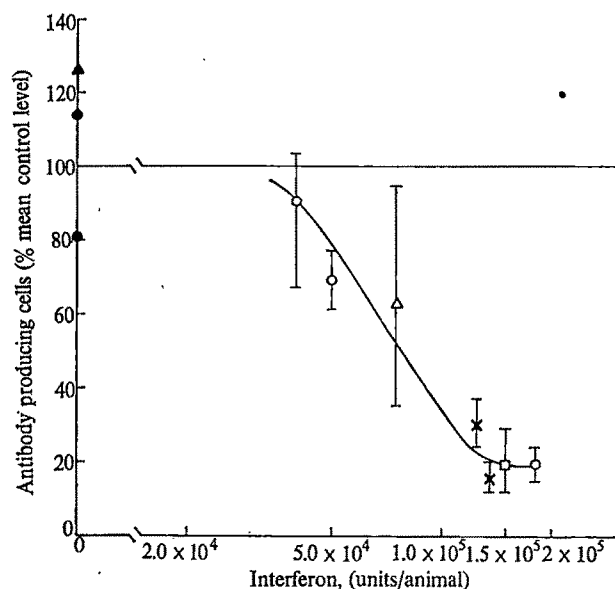


Fig. 2 Relationship of interferon dose and number of antibody producing spleen cells. Animals were sensitized to SRBC antigen by intravenous administration of 2×10^7 SRBC in 0.5 ml saline. Antibody-producing capability was measured by the number of spleen cells producing antibody to SRBC 6 d after antigen administration. Antibody-producing cells were assayed by the plaque technique²¹ as extended for use on microscope slides²² with modifications as previously described⁴. Various doses of interferon were administered 2 d before administration of antigen (SRBC). The number of nucleated spleen cells producing antibody to SRBC was assayed 6 d after antigen administration and expressed as a percentage of the number of antibody producing spleen cells in uninjected controls. All determinations shown represent the mean in at least two animals. Ranges shown are $\pm$ s.d. Two uninduced control preparations containing less than 10 units of interferon were also used. One consisted of pressure dialysed supernatant of L_{929} cell tissue culture medium (●), and the other of serum from untreated mice (▲). Interferon preparations from four sources were used, all induced with NDV. One from L_{929} cells and pressure dialysed 5 to 50-fold (○) (ref. 18), one from C243-3C cells and pressure dialysed 20-fold (×) (ref. 10), one from mouse serum 10 h after injection of NDV (△), and one purified on an anti-interferon affinity chromatography column (□) (ref. 11). Five days of pH 2 treatment was used to inactivate NDV in all interferon preparations and no residual interfering activity as titred in human neonatal fibroblasts was noted in any preparation.

depressant activity (17% of control), while the inactivated preparations showed only activity consistent with their residual antiviral activity (Table 1). To check the species specificity of the depressant activity, 1×10^5 units of human leukocyte interferon were administered to mice with the result that no significant decrease in the number of antibody producing spleen cells was observed (Table 1).

At first the differing effects of interferon inducers such as poly (rI)·poly (rC), which increases the number of antibody producing spleen cells, and interferon preparations which decrease the number of antibody producing spleen cells, seem paradoxical. Recent findings, however, do provide a possible explanation; in addition to inhibition of multiplication of tumour cells, interferon preparations inhibit the multiplication of tissue culture cells in both continuous cell lines^{12,13} and primary cell cultures^{14,15}. Also, interferon preparations have been reported to inhibit DNA synthesis in mouse lymphocyte suspensions stimulated by phytohaemagglutinin¹⁶, and to inhibit proliferation of transferred spleen cells and the ability of these transferred lymphocytes to become sensitized to host alloantigens as assayed by an *in vitro* cytotoxic assay system¹⁷. In view of these findings that interferon depresses cell multiplication, inhibits DNA synthesis in lymphocytes, and otherwise blocks T lymphocyte function, it is not surprising that we should now find that interferon inhibits B lymphocyte expression in response to primary antigen stimulation.

Our results may form grounds for concern with regard to the use of interferon preparations in the treatment of viral infections in humans. It should be noted, however, that circulating interferon titres of the level required to produce these effects are produced transiently during a variety of systemic viral infections in the mouse. Also, concerning the possible clinical usefulness of exogenous interferon, it is important to compare the doses which we find to inhibit antibody producing cells in the spleen with that required to prevent various viral infections. The immunosuppressive doses are approximately 10 to 100-fold greater than that required to prevent a lethal cytotoxic virus infection¹⁸ or virus induced neoplasm¹⁹ in the same species. Previous observation⁹ of an immunosuppressive effect at one twentieth the dosage required in our study could not be confirmed, and further study is needed to elucidate the discrepancy between these two results.

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Changes in the Incorporation of Different RNA Precursors into the Maternal Liver during Pregnancy

DIFFERENT RNA precursors have been utilized to label foetal and maternal RNA *in vivo* with varying results^{1,2}. Recently ³H-cytidine has been shown to effect the highest level of radioactive incorporation into both the maternal and foetal RNA³. The work reported here was undertaken to compare the incorporation of three separate RNA precursors into the rat maternal liver serially throughout gestation; thus, differences in incorporation that may develop with pregnancy among the individual precursors can be compared directly.

Dated pregnant Sprague-Dawley rats (Zivic Miller, Pittsburgh) weighing 200–420 g were used. Two hours after

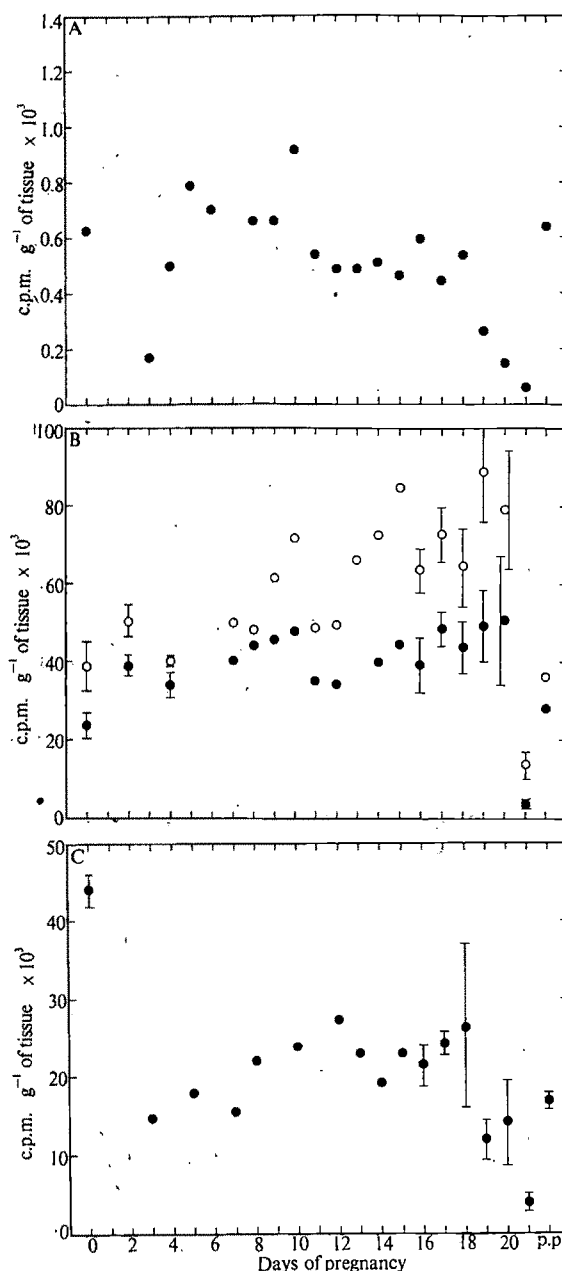


Fig. 1 Incorporation of (A) ³H-uridine (28 Ci mmol⁻¹), (B) ³H-cytidine (6 Ci mmol⁻¹), and (C) ³H-orotic acid (11 Ci mmol⁻¹) into maternal liver 2 h after injection. Bars represent standard error of mean. 0 d pregnancy indicates studies on young male rats. p.p., 24 h post-partum; ○, acid-soluble counts; ●, acid-insoluble counts.

intraperitoneal injection of isotopes (10 μ Ci per 100 g of body weight), the animals were killed by cervical dislocation. A 2.0 g sample of the maternal liver was homogenised in 9 volumes of cold 0.1 M sodium acetate buffer, pH 5.0, using a Potter-Elvehjem homogeniser. One-tenth volume of 50% trichloroacetic acid was added, stirred and centrifuged. The precipitate was washed twice with 5% trichloroacetic acid. A 0.5 ml sample of the pooled washings and the supernatant was placed in 10.0 ml of Bray's solution to measure the level of radioactivity using a liquid scintillation counter. The precipitate was hydrolysed for 15 min in 10 ml of 10% trichloroacetic acid in a boiling water bath, cooled and centrifuged at 10,000g for 10 min. Using 0.5 ml from the resulting supernatant the radioactivity of the acid-insoluble counts was determined in Bray's solution.

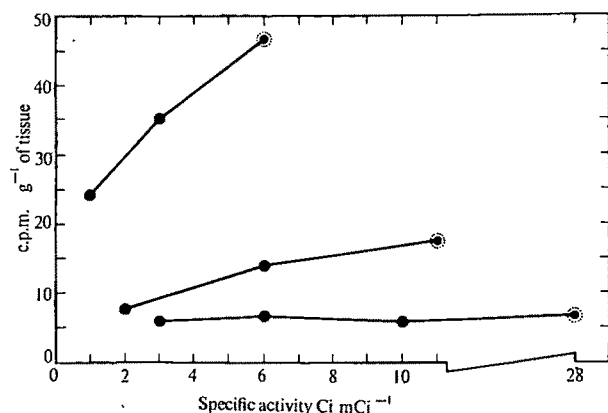


Fig. 2 Incorporation of ^3H -uridine (lower curve), ^3H -cytidine (upper curve) and ^3H -orotic acid (middle curve) into the maternal liver of 16-d pregnant rats with varying specific activities. The experiments were conducted as described in Fig. 1. The total volume of the precursor was kept constant through the study. $\circ$, Represents the specific activity used in experiments shown in Fig. 1.

The 2 h post-injection period was selected since ^3H -cytidine reached maximum incorporation at this time in accordance with a previous study³; whereas ^3H -uridine yielded a consistent and steady level of radioactive incorporation during the same time. The identical 2-h interval was maintained with ^3H -orotic acid only for purposes of comparison since ^3H -orotic acid continued to be incorporated for a longer time.

Figure 1 clearly shows the marked differences in the incorporation of isotopically labelled uridine, cytidine and orotic acid. The non-pregnant rats in this series designated as 0 d represent male rats (170–190 g) because of the wide variations observed from using virgin rats, especially with ^3H -uridine. Additional experiments performed on animals 48 to 72 h after delivery yielded results similar to those noted in the 24 h post-partum group shown in Fig. 1. Thus, the post-partum values may be most representative of the non-pregnant state for comparison with pregnancy. Every point in the figure represents an average of two to three separate animal experiments; when considerable scatter of values was obtained, especially towards the end of pregnancy, an additional six to eight animals were studied to determine the standard error of the mean. Note that early in pregnancy, uridine displayed decreased incorporation while cytidine and orotic acid had values comparable with the post-partum group. Although the orotic acid was incorporated to an unusually high degree among the male rats, cytidine is the most effective during pregnancy, confirming an earlier report³. Uridine was the least efficient precursor in both the pregnant and non-pregnant states, and further experiments revealed no changes in uridine

kinase in the maternal liver during pregnancy. The acid-soluble counts, although graphed only with the cytidine studies, in all cases mirrored the changes observed in the acid-insoluble counts, but the actual values were slightly higher. However, the most dramatic and consistent result was the sharp decrease in the incorporation of all precursors on the twenty-first day of pregnancy, just before parturition. Within 24 h post-partum the level of incorporation returned to earlier pregnant or non-pregnant values.

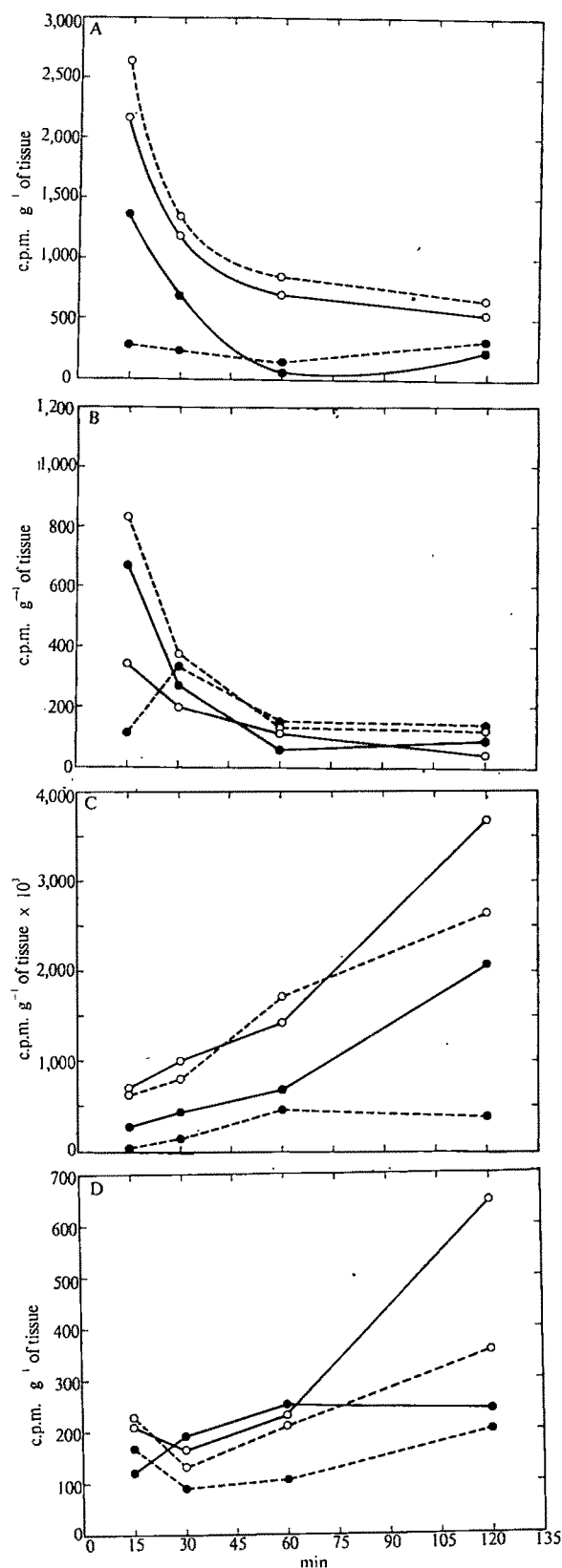


Fig. 3 The incorporation of ^3H -cytidine and ^3H -uridine into the nucleus and cytoplasm of maternal liver during various stages of pregnancy. A and C, Nuclear acid-insoluble counts (uridine); B and D, cytoplasmic acid-insoluble counts (cytidine). Non-pregnant rats represent young male animals. At specific times after intraperitoneal injection of isotopes (10 μCi per 100 g of body weight), the animals were killed. From 4.0 g of liver, 25% homogenate was prepared with 0.1 M sodium acetate buffer, pH 5.0, using Tri-R Homogenizer for ten strokes at 1,200 r.p.m. The homogenate was filtered through four layers of cheese cloth and the nuclear fraction was isolated as a pellet by centrifugation at 700g for 20 min. The nuclear and cytoplasmic preparations were treated with an equal volume of 10% trichloroacetic acid and washed once with 5% trichloroacetic acid. The resulting precipitates were treated and counted as acid-insoluble radioactive counts as described earlier in Fig. 1. $\circ$ — $\circ$, 8 d; $\circ$ — $\circ$, 18 d; $\bullet$ — $\bullet$, 21 d; $\bullet$ — $\bullet$, non-pregnant.

In approximately a quarter of the rats studied, an additional procedure included measurement of radioactivity in the blood. One and a half hours after injection of the labelled precursor, the animals were sedated by intramuscular injection of sodium pentobarbital (30 mg. kg⁻¹). Rats were anaesthetised in an ether chamber just before death 2 h after injection and 3.0 ml of blood was obtained by a direct cardiac tap using a 20 gauge needle and a heparinised syringe. Aliquots of 0.1 ml of plasma were placed in 10.0 ml of Bray's solution to determine radioactivity. The maternal liver was homogenised and prepared as described earlier. The level of blood radioactivity measured in the plasma was relatively constant throughout pregnant and non-pregnant animals with only a slight decrease at 21 d. With orotic acid and uridine the radioactivity measured 40,000 to 55,000 c.p.m. ml⁻¹ of plasma; whereas, cytidine showed only 9,000 to 11,000 c.p.m. ml⁻¹ of plasma.

Figure 2 illustrates the differences in incorporation of 16-d pregnant rats using precursors with varying specific activities. Orotic acid showed a slight rise in radioactivity with increasing specific activities, but cytidine exhibited a marked increase. In direct contrast, uridine showed no change with even greater alterations in specific activities suggesting a rapid saturation of its system. Although the actual measured radioactive counts were considerably lower, a similar pattern of response was observed in 21-d pregnant rats with all three precursors.

Figure 3 demonstrates the marked differences in the incorporation of ³H-uridine and ³H-cytidine into the nuclear and cytoplasmic portions of the liver during various stages of pregnancy. Although the actual amount of radioactive labelling is relatively small by comparison, ³H-uridine is incorporated rapidly into both the nuclear and cytoplasmic RNA and then falls off within 30 min. The 21-d pregnant rat shows poor uptake of radioactivity throughout the 2 h period of observation. The incorporation of ³H-cytidine differs in that the isotopic incorporation in both the nucleus and cytoplasm increases during the 2 h period, in a manner similar to that observed using labelled orotic acid. The 8 and 18-d pregnant rats reveal enhanced labelling compared with the non-pregnant rat, but the 21-d pregnant rat displays

Table 1 Comparison of Specific Activity of Liver RNA Polymerases in 16-d and 21-d Pregnant Rats

	16-d pregnant rats	21-d pregnant rats
	Mg ²⁺ -activated	
Nuclear	131	253
Nucleolar	158	161
Extranucleolar	2,199	1,306
	Mn ²⁺ (NH ₄) ₂ SO ₄ -activated	
Nuclear	116	220
Nucleolar	217	165
Extranucleolar	2,716	1,623

Nuclei were isolated from liver homogenate according to Widnell and Tata⁴, and nucleolar and extranucleolar (nucleoplasmic) suspensions were prepared as described by Yu and Fiegelson⁵. The RNA polymerase assay was essentially the method of Weiss⁶. The reaction mixture contained 50 µmol of Tris-HCl buffer, pH 8.5; 2.5 µmol of magnesium chloride, 3 µmol of sodium fluoride and 10 µmol of cysteine; 0.3 µmol each of GTP, CTP and ATP and 0.015 µmol of UTP; 2.0 µCi of 5-³H-UTP (Schwarz-Mann, 14.0 Ci mmol⁻¹) and 0.1 ml of enzyme suspension. For the ammonium sulphate assay 2.0 µmol of MnCl₂ and 0.2 mmol of (NH₄)₂SO₄ were used instead of MgCl₂ and the pH of the buffer was 7.5 (ref. 7). After incubation for 15 min at 37°C the reactions were stopped, adding 0.10 M sodium pyrophosphate containing RNA and bovine serum albumin⁸. The RNA was collected on Whatman GF C filters and radioactivity measured with liquid scintillation counter using 10.0 ml Bray's solution. RNA determinations were done according to Fleck and Munro⁹. Values represent an average of three determinations and indicate pmol of UMP incorporation per mg DNA.

a markedly depressed level of incorporation as noted in the ³H-uridine experiments.

To exclude the possible effects of changes in the intra-peritoneal absorption of isotopes, the three labelled precursors were administered intravenously through the tail vein to another group of 16-d and 21-d pregnant animals. Again a comparable labelling of the 16-d pregnant and the depressed incorporation of the 21-d pregnant rats were noted as the results show in Fig. 1.

Table 1 summarises our studies on the nuclear, nucleolar and extranucleolar DNA-dependent RNA polymerases from the livers of 16-d and 21-d pregnant rats. The results indicate that there is no drastic decrease in the specific activity of DNA-dependent RNA polymerases in the 21-d pregnant rat in spite of the marked depression in the incorporation of RNA precursors. There is a measurable drop only in the extranucleolar DNA-dependent RNA polymerase.

The specific causes for the changes in the incorporation of the various RNA precursors during pregnancy remains unresolved although endocrine influences must play a dominant role. The work reported here, however, clearly indicates that pregnancy and the duration of pregnancy have profound effects on the degree of RNA incorporation with different RNA precursors.

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Slightly Deleterious Mutant Substitutions in Evolution

RECENT advances in molecular genetics have had a great deal of influence on evolutionary theory, and in particular, the neutral mutation-random drift hypothesis of molecular evolution^{1,2} has stimulated much interest. The concept of neutral mutant substitution in the population by random genetic drift can be extended to include random fixation of very slightly deleterious mutations which have more chance of being selected against than of being selected for^{3,4}. If this class of mutant substitution is important, we can predict that the evolution is rapid in small populations or at the time of speciation⁵. Here I shall organize the observed facts which indicate that this class is in fact important.

Fitch and Margoliash⁶ have shown that the frequency of double fixation of mutants in a leg of their cytochrome c phylogenetic tree is higher than predicted from chance. The

most plausible interpretation is that the first mutant is slightly deleterious and that the second compensates for the first. This interpretation makes Fitch's concept of the covarion⁷ most easily understood. If the first mutant disturbs very slightly the normal function of the molecule, there are probably many ways of compensating, and so the first mutant provides a new possibility for evolutionary change. This is considered to correspond to Fitch's observation of unstable covarions⁷.

The evolution of tRNA follows the same pattern. It is known that evolution is more rapid in the paired region than in the non-paired region of tRNA⁸. In most tRNAs, the paired region is almost exactly paired, therefore there must have been coupled substitutions in evolution as first mentioned by Jukes⁹. Dayhoff and McLaughlin⁸ state "this could be explained by an oscillatory sequence of evolutionary events, involving first a single base change that weakens the bonding, followed by a second change which restores the hydrogen-bond pairing". It is hard to conclude from this that each sequence has evolved so as to fit better into its environment. It indicates rather that the first substitution is slightly deleterious. This idea can be extended to other protein molecules, particularly if the polypeptide-folding mechanisms are important, as discussed by Barnard *et al.*¹⁰. Any amino acid substitution of a well organized molecule is likely to disturb the organization, but once it spreads in the population by random drift, it opens the way for further evolutionary change.

This hypothesis is compatible with a different point of view, that is, frequency distribution of multiple alleles detected by electrophoresis. Several investigators have been trying to prove or disprove the neutral theory of protein polymorphisms by looking at the pattern of allelic distribution^{11,12}. In such attempts, it is usually assumed that every mutant appearing in the population is one not pre-existing, that is to say, the so called "infinite allele model" of Kimura and Crow¹³ has been used extensively. The convenient statistics often used in the analysis are the effective number of alleles (n_e ; reciprocal of the sum of squares of allelic frequencies) and the actual number of alleles observed (n_a). Recently, Yamazaki and Maruyama¹⁴ made an extensive compilation and statistical analysis of published data on enzyme polymorphisms. In particular, they showed that the average ratio of the effective to the actual number of alleles (n_e/n_a) from the observed enzyme polymorphisms agrees well with the neutral hypothesis according to Kimura and Crow's infinite allele model. Here the ratio, n_e/n_a , represents a sort of evenness of allele distribution and, the higher the ratio, the more uniform the distribution expected. But this model seems to be inappropriate for electrophoretically detectable polymorphisms, for this method can only detect a difference in the electric charges of molecules as discrete bands on the gels. In fact Bulmer¹⁵ noticed non-random arrangements of electrophoretic bands of common and rare alleles. In view of these points, Maynard Smith¹⁶ and Kimura and Ohta¹⁷ have suggested that the model of stepwise allele production is more appropriate. Using this mutational scheme but assuming an infinite number of possible states, we have shown that the effective number of neutral alleles maintained in a finite population becomes, $n_e = \sqrt{(1 + 8N_e v)}$, where N_e is the effective population size and v is the mutation rate per gamete¹⁸. When $N_e v$ is large this formula gives a smaller effective allele number than that predicted by Kimura and Crow's model. Furthermore, the frequency distribution of multiple alleles is influenced significantly. We have performed extensive Monte Carlo experiments and have shown that the ratio of the effective to the actual number of alleles (n_e/n_a) is larger in the step allele model, particularly when n_a is large (T. O. and M. Kimura, unpublished). Then the agreement between the observation and Kimura and Crow's model shows that there exist more rare alleles than expected from the strict neutral hypothesis. From this, I conclude that rare alleles are on the

Table 1 Relationship between Substitution Rate in Small Populations and Equilibrium Frequency in Large Populations of Slightly Deleterious Mutations

Homozygous disadvantage	Equilibrium frequency in large populations	Rate of substitution in proportion of the completely neutral case	
		$N_e = 10^2$	$N_e = 10^3$
Recessive deleterious			
10^{-2}	0.032	0.43	0.8×10^{-7}
10^{-3}	0.1	0.94	0.43
10^{-4}	0.32	0.99	0.94
Semidominant deleterious			
10^{-2}	0.002	0.31	0.5×10^{-7}
10^{-3}	0.02	0.90	0.31
10^{-4}	0.2	0.99	0.90

The mutation rate is assumed to be 10^{-5} .

average selected against. The alleles, which can increase their frequency up to several per cent in very large populations like *Drosophila* species, can replace the previous allele in small populations by random drift.

O'Brien *et al.*¹⁹ reported that the "null" alleles at the α -glycerophosphate dehydrogenase-1 locus of *Drosophila melanogaster* are deleterious. As their null alleles were induced by EMS, they may be different from those observed in low frequencies in natural populations. It is likely, however, that the null alleles are generally deleterious. They can replace the previous allele in a bottleneck population. Vitamin requirement is in fact considered to be the result of such procedures. King and Jukes⁹ noticed that lack of vitamin C is always associated with the kind of food and they consider that, when selective constraints are reduced, the genes for vitamin C have deteriorated.

As an example, suppose that the homozygous disadvantage of the recessive deleterious mutant is 10^{-4} . If the mutation rate is 10^{-5} , the equilibrium mutant frequency is 10% in large populations. By using Kimura's²⁰ formula for the fixation probability of mutant genes, the rate of substitution of this slightly deleterious mutant becomes 0.43×10^{-5} per generation if the effective population size is 10^3 . This corresponds to 43% of the substitution rate of the strictly neutral case. Table 1 illustrates such examples in terms of the proportion of the substitution rate of the completely neutral case.

I have previously suggested the possibility of slightly deleterious mutant substitutions in cistrons in view of the apparently contradictory observation of generation-dependent DNA evolution against year-dependent cistron evolution⁴. Together with the supporting observations presented here, I suggest that very slight genetic deterioration might play an important role in molecular evolution. Here, organization at a much lower level in each molecule or in several interacting molecules could provide a clue to understanding the evolutionary change at the molecular level, rather than cohesive interaction of the pool often postulated by orthodox neo-Darwinism²¹. It seems from the report of Mukai *et al.*²² that there is no evidence that alleles at different loci constitute such interaction systems or "super genes". I thank Dr M. Kimura for discussions.

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Antitumour Activity of Iodine in Acidic Medium with Calcium

THE basal metabolism is increased in many patients with lymphatic and myelogenous leukaemia. Elevated levels of plasma iodine have been found in various leukaemic cases, possibly indicating involvement of the thyroid gland¹. It is thought that at lower pH values there is more free iodine, and so greater penetrability into cells and greater iodine activity². Iodine fixation by human leukocytes requires energy³. Iodine alters the redox state of the cytoplasm and mitochondria, because the couple $2\text{I}^- \rightarrow \text{I}_2 + 2\text{e}^-$ has a rather high redox potential: +0.535 V; iodine seems to be one of the oxidizing agents which can be used for ATP formation⁴. Flavin is the most likely oxidizing agent for a couple with such a higher redox potential⁵.

The importance of calcium ions in controlling the permeability of cells⁶ and in regulating cellular activity⁷ has been established. The penetration of isolated ascites tumour cells by calcium ions depends on the metabolic state of the cells⁸; calcium accumulation, like iodine accumulation, requires energy and alters the redox state of the respiratory chain components.

It has been suggested that iodine in acidic medium with calcium has antitumour activity (L. Heinonen, personal communication). We therefore studied the effect of these substances against myelocytic chloroleukaemia⁹. This leukaemia was induced in 2 to 3-week-old Sprague-Dawley and Wistar rats by intraperitoneal or subcutaneous inoculation. Chloroleukaemic cells were suspended in physiological saline and 0.1 ml of the cell suspension, containing 10,000–20,000 cells, was injected into the rats. Survival time, histological examination and lactic acid dehydrogenase (LDH) activity were used to evaluate antitumour activity.

Treatment was started 24 h after the intraperitoneal inoculation by giving each rat about 500 μg of iodine daily as a 5% iodine-ethanol solution in cultured milk. Fourteen days after the inoculation the treatment with iodine was continued by subcutaneous injection. Treatment of the subcutaneously induced local tumours was by subcutaneous injection of iodine, starting about two weeks after inoculation, when the tumour was clearly visible and was usually about 2 cm $\times$ 3 cm, sometimes larger. The subcutaneous injections consisted of 500 μg of iodine in ethanol solution mixed with 1 ml of liver extract (Pernaemon forte, N.V., Organon, Oss, Netherlands). Immediately afterwards 1 ml of calcium gluconolactobionate solution (about 9 mg Ca^{2+}) (Calcium Sandoz, Sandoz AG, Basel, Switzerland) was injected intramuscularly. The injections were made once (intraperitoneally inoculated rats) or twice (subcutaneously inoculated rats) daily. Eleven days after

inoculation the intraperitoneally inoculated rats were injected with 25 mg of thiamine chloride (Neuramin forte, Orion Ltd., Espoo, Finland).

The rats' food consisted of vegetables, including cabbage and carrots, and fresh liver, with 3 mg riboflavin (Orion Ltd., Espoo, Finland) per rat per day. The control rats were given all the nutrients, liver extract, calcium and vitamins but not iodine.

Tissue samples were taken at autopsy not only from the visible tumours but also as a routine procedure from liver, spleen, kidney, lung, heart and bone marrow. After fixation in formalin the tissue samples were cut into sections 6 μm thick and stained with haematoxylin-eosin. The smear samples of femoral bone marrow were stained by the May-Grünwald-Giemsa method. The preparations were examined under a light microscope. LDH activity was estimated by measuring the extent of oxidation of NADH (at 340 nm).

Table 1 shows the effect of treatment on the survival time of the rats bearing a tumour inoculated intraperitoneally or subcutaneously. The index $T/C \times 100$ [(mean survival time of treated rats)/(mean survival time of untreated control rats) $\times 100$] was calculated to be >415 for the intraperitoneally inoculated rats. This is three to four times higher than the ratio reported by other workers^{10–12}. Our result might have been even better if the iodine administration had been by injection from the start of the experiment, as we found that the rats did not drink all of their iodine-containing cultured milk. The index was not calculated for the subcutaneously inoculated rats because the tumours had disappeared before the rats were killed (Tables 1 and 2). The average survival time

Table 1 Influence of Iodine Treatment on Survival Time

Intraperitoneally inoculated rats					
Rat	Survival time <i>T</i> (d after inoculation)	<i>T/C</i> × 100	Cause of death	No. of treat- ments	Dose of iodine (μg d ⁻¹)
Treated rats					
a	> 61	> 555	Killed	25	500
b	28	255	Died	17	500
c	17	155	Died	3	500
d	> 61	> 555	Killed	25	500
e	> 61	> 555	Killed	26	500
Untreated control rats					
f	12		Died	—	—
g	12		Died	—	—
k	9		Died	—	—
Subcutaneously inoculated rats (local tumour)					
Rat	Survival time (d after inoculation)	Cause of death	No. of treat- ments	Dose of iodine (μg d ⁻¹)	Disappear- ance of the local tumour (d)
Treated rats					
II†	> 198	Killed	68	625	14
q‡	> 33	Killed	35	1,000–4,500	†
r	> 33	Killed	24	1,000	3
s	> 33	Killed	13	1,000	2
v	> 33	Killed	12	1,000	3
Untreated control rats					
p	> 33	Killed	—	—	—
XI	24	Died	—	—	—
j	35	Died	—	—	—
ö	34	Died	—	—	—
y	35	Died	—	—	—
z	41	Died	—	—	—

* C, Mean survival time of untreated control rats (f–k) = 11 d and of untreated control rats (XI–z) = 34 d.

† Rat II received iodine in cultured milk during the whole experimental period.

‡ Rat q received a more concentrated iodine-liver extract daily (1,000 to 4,500 μg of iodine ml^{-1}). The tumour underwent alteration to fatty necrosis.

of the control rats inoculated subcutaneously was 34 d from inoculation, somewhat longer than the survival time reported by Rytömaa and Kiviniemi¹³. All the five rats with local tumours became healthy after iodine treatment, and eight out of the total number of ten treated rats recovered, whereas eight out of the nine untreated control rats died.

Table 2 Effect of Treatment on the Size of Subcutaneously Induced Tumours

Rat	Diameter of tumour at beginning of treatment (cm)	Fate of tumour
Treated rats		
II		Complete disappearance in 14 d
q	2.8*	Transformation to fatty necrosis
r	2.0†	90% reduction in 2 d, complete disappearance in 3 d
s	1.5	Complete disappearance in 2 d
v	2.5	Complete disappearance in 3 d
Untreated control rats		
p	2.8	Growth ceased after 5 d
j	2.8	Growth continued
XI	1.5	Growth continued

* This tumour was treated by pouring over the tumour a large amount of iodine in liver extract, followed by the calcium solution.

† Two subcutaneous inoculations resulted in two tumours that grew together over the neck for a length of 4 cm.

The histological findings are presented in Table 3. Leukaemic infiltrations were found in only two of the ten treated rats. In the untreated group of eight rats there was tumour tissue in seven animals. Recovery was 100% from subcutaneously induced tumours and 60% from intraperitoneally induced tumours. One local large tumour (rat q) was treated by pouring over the tumour a large amount of iodine in liver extract, followed by the calcium solution. In its histological examination only fatty necrosis was seen. During the recovery of the treated rats the number of erythrocytes, the haemoglobin value, and the packed cell volume attained normal levels.

Elevated LDH activity has been found in a variety of tissue tumours and in acute and chronic myelocytic

leukaemia¹⁴. We measured the LDH activity in the pooled peripheral blood of treated rats (Table 4). In the rats with subcutaneous tumours the activity of LDH decreased during the treatment and was close to, though still above, the control value for normal healthy rats at the end of the treatment. The two leukaemic rats which did not recover are presumably the source of the elevated value in the pooled samples. The effectiveness of iodine in lowering LDH activity may be due to the fact that iodine rapidly oxidises the SH groups of LDH¹⁵, inhibiting the enzyme activity.

Table 4 LDH Activity in Peripheral Blood During the Treatment

Form of leukaemia	Stage of treatment			Duration of experiment (d)
	Beginning (before treatment)	Middle	End	
Intraperitoneally inoculated	8,000 (<i>n</i> =0)	6,490 (<i>n</i> =3)	4,630 (<i>n</i> =11)	5
Subcutaneous tumour	2,140 (<i>n</i> =0)	460 (<i>n</i> =10)	860 (<i>n</i> =16)	16
Normal healthy rats	720 (<i>n</i> =0)		650 (<i>n</i> =0)	16

n, No. of treatments.

LDH activity is given in Wroblensky units per ml.

Four rats on average were used for each determination.

The average body weight of the intraperitoneally inoculated and treated rats increased gradually from 30 g to 195 g in the month following inoculation, while the untreated rats showed only a small increase in weight (22 g) during their lifetime. After the disappearance of the local tumours from the subcutaneously implanted rats, their weight increased normally.

From these results it can be concluded that iodine in acidic medium with calcium has a remarkable activity against myelocytic chloroleukaemia. Iodine may act on the electron transport chain: mitochondria in tumour cells differ morphologically and functionally from normal cells. Most suggestions for the mechanism of action of anti-tumour agents have involved inhibition of DNA and protein synthesis, whereas we suggest that iodine acts by changing the redox state inside the cell.

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Table 3 Histological Findings in Different Organs at Autopsy of Treated and Untreated Rats Inoculated Intraperitoneally or Subcutaneously with Leukaemic Cell Suspension (Myelocytic Chloroleukaemia)

Leukaemic infiltrations	Treated rats		Total No. of rats
	Intraperitoneal inoculation (rats: a, b, c, d, e) No. of rats	Subcutaneous inoculation (rats: II, q, r, s, v) No. of rats	
Yes	2	—	2
No	3	5	8
Total	5	5	10
Leukaemic infiltrations	Untreated control rats		Total No. of rats
	Intraperitoneal inoculation (rats: g, i, k) No. of rats	Subcutaneous inoculation (rats: p, XI, ö, y, z) No. of rats	
Yes	3	4	7
No	—	1	1
Total	3	5	8

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Vitamin D-induced Synthesis of mRNA for Calcium-binding Protein

THE discovery that vitamin D must first be converted into the metabolites 25-hydroxycholecalciferol¹ (25 OH-D₃) and 1,25-dihydroxycholecalciferol² (1,25(OH)₂-D₃) before calcium absorption across the small intestine is enhanced has radically changed existing ideas as to the mode of action of vitamin D. Indeed, it is now well established that the most active metabolite of vitamin D for calcium absorption, 1,25(OH)₂-D₃, is produced solely by the kidney³ and that its production and secretion are under very fine endocrine control. This finding, together with the observation that 1,25(OH)₂-D₃ is specifically located in the nucleus of the target cell⁴ and the apparent involvement of RNA and protein synthesis⁵⁻⁷ in the intestinal action of vitamin D, provide the basis of the proposal that 1,25(OH)₂-D₃ can be classed as a steroid hormone.

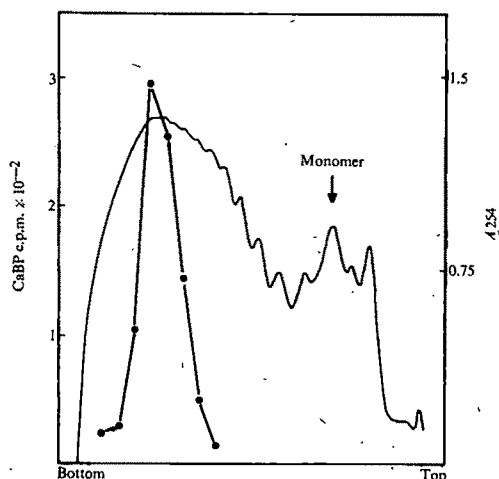


Fig. 1 Size of CaBP-synthesizing polysomes. 1 mg (20 A_{260} units) of polysomes from intestinal cells of vitamin D₃-dosed chicks was layered on a 15 to 45% sucrose gradient in 25 mM NaCl, 25 mM Tris-HCl, pH 7.5, 5 mM MgCl₂ and centrifuged in the SW 36 rotor for 100 min at 2° C and 35,000 r.p.m. Fractions were collected as indicated and RNA extracted and translated in the lysate as described in Table 2. ●, CaBP synthesizing polysomes; —, polysome profile.

The role of 1,25(OH)₂-D₃ as a steroid hormone implies that it acts at the level of gene transcription. We have tested this hypothesis by investigating the synthesis of calcium binding protein (CaBP), formed in response to vitamin D⁸. More specifically, we have sought to determine whether CaBP is synthesized *de novo* or formed from an inactive precursor as proposed by Drescher and DeLuca⁹ and whether the action of 1,25(OH)₂-D₃ on the nucleus promotes the formation of a specific mRNA for CaBP.

Table 1 Effect of Vitamin D on the Synthesis of CaBP by Isolated Polysomes

Source of polysomes	TCA insoluble d.p.m. in released protein	Radioactivity in immunoprecipitate (d.p.m.)
Rat liver	56,000	330
Chick intestinal mucosa (-D)	51,200	270
Chick intestinal mucosa (+D)*	64,000	4,475

* Rachitic chicks received 5 µg vitamin D₃ 72 h before being killed.

Polysomes were isolated as described¹⁰. *In vitro* polypeptide synthesis was conducted at 37° C in a medium containing 1 mM ATP, 0.4 mM GTP, 10 mM creatine phosphate, 40 µg ml⁻¹ creatine kinase, 50 µM of each amino acid except leucine, 0.5 µCi ml⁻¹ ³H-leucine, 0.2 to 0.5 mg ml⁻¹ polysomal RNA, 0.2 ml ml⁻¹ gel-filtered rat liver cell sap, 1 mM dithiothreitol and 20 mM Tris-Cl, pH 7.5. Optimal ionic concentrations were 4 mM MgCl₂ and 100 mM KCl. After 30 min incubation, ribosomes were removed by centrifugation at 150,000g (maximum) for 4 h to produce a supernatant containing released protein. Trichloroacetic acid (TCA) precipitable radioactivity was measured as described by Mans and Novelli¹⁴. Immunoprecipitates were washed twice and dissolved in 0.2 ml NCS tissue stabiliser for scintillation counting.

Table 2 Synthesis of Immunoprecipitable Protein in a Rabbit Reticulocyte Lysate Programmed with Intestinal RNA

RNA added	Total radioactivity incorporated (c.p.m. per 10 µl)	¹⁴ C precipitated by anti-CaBP (c.p.m.)
None	14,200	149
150 µg (-D)	13,700	155
108 µg (+D)*	14,300	361
216 µg (+D)*	14,000	551

* Rachitic chicks received 5 µg vitamin D₃ orally 72 h before being killed.

Incubation conditions for the lysate were as described¹⁵ except that ATP and GTP were omitted and MgCl₂ and creatine phosphate were present at 0.5 mM and 10 mM respectively; the concentration of non-radioactive leucine was 50 µM and ¹⁴C-leucine was 2.5 µCi ml⁻¹. Incubations were carried out at 30° C for 60 min in a volume of 500 µl and contained the amounts of intestinal RNA shown above. After incubation, a 10 µl sample was taken to measure TCA insoluble radioactivity¹⁶; the remainder was made 1% with Triton-X100 and deoxycholate and 10 mM with leucine. Non-radioactive CaBP (10 µg) and excess antiserum were then added to the mixture and, after 30 min at room temperature, the immunoprecipitate was collected by centrifugation through M sucrose¹¹ and dissolved in NCS tissue solubiliser.

The first question was answered by investigating the ability of polysomes isolated from rachitic and vitamin D₃-dosed chicks to synthesize CaBP in an *in vitro*, cell-free system. Chick intestinal polysomes were isolated from a post-mitochondrial supernatant by sedimentation through a 0.5 M/2.0 M discontinuous sucrose gradient as previously described¹⁰ and incubated as shown in Table 1. After the

incubation, the ribosomes were removed by centrifugation and the incorporation of ^3H -leucine into completed polypeptide chains and into CaBP was determined. The specificity of the precipitin reaction used to quantify CaBP synthesis has already been reported¹⁰. It is clear from Table 1 that tritium is incorporated into CaBP by polysomes isolated from vitamin D₃-dosed chicks. On the other hand, polysomes both from rachitic chick intestinal cells and from rat liver cells resulted in the same low level of radioactivity in the immunoprecipitate. We interpret these results as *de novo* synthesis of CaBP.

We wished to test directly the production of a specific mRNA as a result of vitamin D administration. RNA was prepared from intestinal polysomes (for method see ref. 11) and incubated in a rabbit reticulocyte lysate¹⁵. Table 2 shows that RNA preparations from intestinal polysomes of vitamin D-dosed chicks directed the *in vitro* synthesis of a product which is precipitable by our specific antiserum. RNA from rachitic chick intestinal polysomes was devoid of this activity.

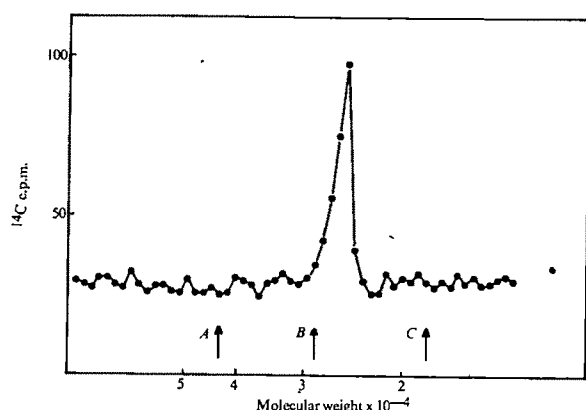


Fig. 2 Sodium dodecylsulphate-acrylamide gel electrophoresis of anti-CaBP precipitable radioactivity. RNA from the peak fraction of Fig. 1 was translated in the lysate and the immunoprecipitable radioactivity recovered as described in Table 2. The immunoprecipitate was dissolved by heating to 100°C for 4 min in a sodium dodecylsulphate-Tris-dithiothreitol solution¹⁷ and then electrophoresed on sodium dodecylsulphate-acrylamide gels. Gels were prepared as described by Laemmli¹⁸ except that the concentration of bis-acrylamide was doubled. Electrophoresis was at 5 mA per gel for 100 min. After electrophoresis, 1 mm slices were cut and incubated at 50°C for 2.5 h with 500 μl NCS tissue solubiliser and 30 μl H₂O. After cooling, they were counted in a 10 ml toluene scintillator. Also shown in the figure are the electrophoretic mobilities of, A, ovalbumin (molecular weight 43,000); B, carbonic anhydrase (molecular weight 29,000); C, myoglobin (molecular weight 17,300) on parallel gels.

It was also of interest to determine the size of the CaBP-synthesizing polysomes as well as the molecular weight of the protein produced by the lysate. Thus, intestinal polysomes were fractionated on a sucrose gradient and RNA prepared, as described above, from the fractions. This RNA was translated in the lysate and immunoprecipitable material recovered. Figure 1 displays the polysome profile and the distribution of the CaBP-synthesizing polysomes. It can be seen that CaBP is synthesized on polysomes containing between eleven and fourteen ribosomes. This finding was rather surprising as ovalbumin (387 amino acids)¹² is synthesized on polysomes of the same size¹³. Indeed, we expected to find that CaBP (206 amino acids)⁶ was synthesized on polysomes containing six to eight ribosomes. This anomaly may be explained by postulating that either elongation is rate limiting or that a larger protein is produced and then cleaved after or during synthesis to yield an active CaBP. These possibilities are at present under investigation.

Finally, an experiment was performed to characterise the protein synthesized under the direction of intestinal RNA.

When this RNA was added to the lysate and the resulting antibody precipitate analysed by electrophoresis on SDS-acrylamide gels, a single peak of radioactivity was observed (Fig. 2). Moreover, the mobility of this peak corresponded to a molecular size of 26,000 daltons and was similar to that of authentic CaBP electrophoresed on parallel gels. The absence of a peak of radioactivity with a large molecular weight argues against the precursor molecule discussed above.

We have demonstrated the *de novo* synthesis of a protein having similar molecular and antigenic properties as the intestinal CaBP. The ability to synthesize this protein resides in both polysomes and RNA of intestinal cells from vitamin D₃-dosed chicks; polysomes or RNA from rachitic chicks do not possess this ability. Thus, this study supports the concept that the active metabolite of vitamin D acts in an analogous fashion to the classical steroid hormones.

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Abrogation of Lymphocyte Trapping by Ascitic Tumours

SEQUESTRATION of lymphocytes within antigen-stimulated lymphoid organs is observed regularly following injection of immunogens and adjuvants¹⁻⁵. This lymphoid "trapping" is one of the earliest events in immunization and may be necessary for the expression of an effective immune response. The

mechanism responsible for controlling the operation of the "trap" is incompletely understood but must relate to the way in which lymphocytes normally recirculate.

We have observed defective lymphocyte trapping in animals bearing ascitic tumours. This defect could be transferred to normal animals by injections of cell-free ascitic fluid from animals bearing tumours. The abrogation of trapping applied not only to the tumour but to all immunogens and adjuvants tested. These observations may have relevance to the immunosuppressed state widely recorded in animals and humans bearing advanced tumours⁶⁻⁸ and to the ineffective immune response towards the tumour itself.

The method used to demonstrate lymphocyte trapping has been described in detail elsewhere¹⁻³. The extent to which lymphocytes are sequestered within antigen-stimulated lymphoid organs is measured by determining localization of ⁵¹Cr-labelled syngeneic lymph node cells 24 h after intravenous injection into animals bearing tumours or challenged with antigen. The extent of trapping is reflected by the degree to which the lymphocytes are retained in stimulated lymphoid organs in excess of the localization in untreated controls.

Groups of Balb/c mice received either 10⁷ S37 or 5 × 10⁷ Meth/A sarcoma cells intraperitoneally or were uninjected. At four daily intervals thereafter radio-labelled syngeneic lymph node cells were injected intravenously into representatives of each group and the localization of label determined 24 h later. Animals bearing intraperitoneal tumours had considerably greater localization of labelled cells in their spleens on days 1 and 2 than controls (Table 1). The distribution of labelled cells became identical to that in the controls by day 2 in the Meth/A bearing animals and by day 3 in the S37 bearing animals. (The difference of 1 d between the groups may be related to the higher dose of Meth/A tumour cells used.) Therefore in spite of the continued presence of antigenic tumour, trapping in the spleen was evanescent.

When Balb/c mice received subcutaneous implants of either tumour, augmented localization of radio-labelled cells

occurred in the draining lymph nodes. In contrast to animals bearing ascitic tumours, trapping in this case did not decay but was continuously present for as long as 40 d following implantation. Furthermore, these animals were still able to "trap" when challenged with antigen intravenously (spleen) or subcutaneously (contralateral nodes).

The failure of splenic trapping in mice bearing ascitic tumours for more than 48 h might be explained in several ways. The rapid multiplication of tumour cells in the peritoneal cavity could induce immunological non-reactivity to tumour antigen; trapping is known not to occur in tolerant mice⁹. In this case the loss of trapping would be immunologically specific. Alternatively the presence of intraperitoneal tumour might exert some general effect on the kinetics of lymphocyte circulation. To differentiate between these possibilities animals bearing ascitic tumours were challenged with antigens known to be highly effective in eliciting trapping¹⁻³ and their responses compared with those of normal controls (Table 2). The intravenous injection of sheep erythrocytes (sheep RBC), keyhole limpet haemocyanin (KLH) or Salmonella "H" antigen caused marked sequestration of radio-labelled lymphocytes in the spleens of normal animals. Animals which bore ascitic tumours (4 d after inoculation) could not produce this response. (Although not shown in Table 2, this ability to cause failure of trapping was demonstrated with Meth/A tumour as well.) A similar discrepancy was found after subcutaneous challenge with the same battery of antigens: animals bearing ascitic tumours did not show trapping in the antigen-stimulated lymph nodes.

The latent interval between peritoneal tumour administration and trapping abrogation was indirectly related to the dose of injected tumour cells. Animals receiving an initial dose of 10⁶ tumour cells continued to trap for 5 d, whereas at a high dose of tumour (10⁷ cells) trapping ceased by day 3. Antigen challenge in these animals showed a non-specific failure of trapping by day 4 in the animals given 10⁷ tumour cells. In animals given 10⁶ tumour cells the subcutaneous challenge by antigen failed to initiate trapping by day 7 while intravenous trapping failed by day 9.

Table 1 The Effect of Injection of Intraperitoneal Tumour on Lymphocyte Trapping

	Day 1		Day 2		Day 3		Day 4	
S37 sarcoma	Control	IP tumour	Control	IP tumour	Control	IP tumour	Control	IP tumour
% Localization of labelled cells in the spleen	17.2 ± 0.9	28.1 ± 1.3	16.5 ± 0.5	22.0 ± 1.5	12.6 ± 0.1	11.8 ± 0.3	12.6 ± 0.5	8.6 ± 0.6
% Trapping		63		33				
Meth/A sarcoma								
% Localization in the spleen	17.8 ± 1.0	23.8 ± 1.6	18.5 ± 2.5	20.0 ± 2.4	15.9 ± 0.8	16.2 ± 1.2		
% Trapping*		33		12		0		

Groups of mice injected with 10⁷ S37 or 5 × 10⁷ Meth/A tumour cells on day 0. On days 1-4 control and tumour-bearing animals were injected with ⁵¹C-labelled lymphocytes and the percentage of splenic localization of these cells was determined.

* Trapping of less than 20% is not considered significant.

Table 2 The Failure of Lymphocyte Trapping in Ascitic Tumour-bearing Mice (4 d)

	No antigen		Sheep RBC		Keyhole limpet haemocyanin		Sal. H suspension	
S37 tumour	Control	Tumour bearers	Control	Tumour bearers	Control	Tumour bearers	Control	Tumour bearers
% Localization in the spleen	15.3 ± 0.7	18.6 ± 0.6	27.7 ± 1.6	19.8 ± 0.3	28.2 ± 0.4	16.5 ± 0.6	25.4 ± 0.7	16.8 ± 0.4
% Trapping			81%	0	84%	0	66%	0

Mice bearing ascitic tumour (10⁷ given intraperitoneally on day 0), and controls, were challenged with SRBC, KLH or Sal. H given intravenously 1 h before labelled lymph node cells.

Table 3 The Failure of Lymphocyte Trapping in Supernatant Treated Animals

% Localization of labelled cells	Antigenic challenge		
	No antigen	Subcutaneous sheep RBC	Intravenous sheep RBC
Left lymph nodes	2.6±0.1	2.1±0.1	
Right lymph nodes	2.7±0.2	2.1±0.1	9.1±0.9
Mesenteric lymph nodes	7.1±1.1	4.9±0.3	
Spleen	18.0±1.0	15.1±0.3	19.7±0.9
Liver	28.4±1.8	23.2±0.9	17.1±0.6

Three groups of Balb/c mice were treated with 0.5 ml ($\times 3$) of supernatant raised by injection of 10^7 Meth/A tumour cells in syngeneic hosts. Animals were then challenged with antigen, subcutaneously, on day 3 and intravenously on day 4: one group was left unchallenged. ^{51}Cr -labelled lymph node cells were injected on day 4 and their percentage localization determined on day 5.

Because failure of lymphocyte trapping occurred only in animals bearing intraperitoneal tumour and affected responses not only locally but also in peripheral sites, we considered that the effect might be mediated by some tumour cell product or host factor liberated into the ascitic fluid. To test this, ascitic fluid from tumour-bearing mice was removed and centrifuged to remove cells in suspension. The cell-free supernatant was injected in varying dosages either intravenously or subcutaneously into normal Balb/c mice which were then challenged with antigen or adjuvants known to elicit trapping in untreated controls. Animals which received ascitic fluid supernatant failed to show trapping either in the spleen after intravenous antigen challenge or in the draining lymph nodes after subcutaneous antigen challenge (Table 3). Abrogation of subcutaneous trapping was observed after as little as three daily 0.1 ml intravenous doses of supernatant or a single intravenous injection of 0.3 ml. The consistent abrogation of splenic trapping requires a somewhat higher dose of supernatant, 1 ml $\times 1$ or 0.5 ml $\times 3$. This effect lasted between 24 and 48 h after three pulses of supernatant. Animals treated with supernatant also failed to demonstrate trapping in the regional lymph nodes when challenged with subcutaneous inoculation of the same tumour.

Preliminary observations suggest that the activity present in cell-free ascitic fluid supernatant is preserved after heating or freezing. Samples heated to 56° C for 30 min, or stored at -20° C for up to 3 months, or spun at 100,000g for 3 h, were still active in ablating trapping. The activity is also known to cross allogeneic barriers, that is, supernatant raised in Balb/c mice is effective in abrogating trapping in C3H mice.

If the ability to recruit lymphocytes is important for initiation of immune responses then interference with this mechanism should produce an immunosuppressive effect. The survival of DBA skin grafts on Balb/c mice was prolonged when graft recipients were treated with ascitic supernatant. The median survival time of such grafts in mice treated with 0.3 ml amounts of supernatant for 3 d was 16 d compared with 12 d in untreated controls (unpublished).

These results establish that animals bearing ascitic sarcomas develop impaired ability to recruit lymphocytes after antigen challenge. This defect is immunologically non-specific and can be adoptively transferred to normal animals by a cell-free ascitic fluid supernatant. Such a defect would be expected to result in impaired immune responsiveness, a prediction tentatively supported by the preliminary results of allogeneic skin grafting.

The observation that ascitic fluid from animals bearing tumours may have immunosuppressive properties is not new. Depression of the response to sheep erythrocytes by the administration of tumour ascitic fluid has been reported *in vivo* by Yamazaki *et al.*¹⁰ and *in vitro* by Chan and Sinclair¹¹. Apfel *et al.*¹² found that daily aspiration of ascitic fluid had a protective effect against tumours, and Groshman

and Nowotny¹³ reported that ascitic fluid antagonized the protective effect of endotoxin on tumour growth.

Whether the alteration in lymphocyte kinetics induced by tumour ascitic fluid is directly responsible for immunosuppression remains to be established. These observations offer, however, a possible explanation for the generalized depression of immune responsiveness widely recorded in animals and man with advanced cancer and provide a method for investigating this phenomenon. Moreover, these results suggest yet another mechanism whereby some tumours may escape or render ineffective the immune surveillance and destructive defence of the host. The extent to which these speculations apply to some or all tumours remains to be elucidated.

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New Histone Kinases in Nuclei of Rat Tissues

THE presence of acid-stable phosphomonoesters, principally as phosphoserine, in histones has been reported by several investigators¹⁻⁴, and histone kinases which phosphorylate serine in histones I and IV have been studied widely⁵⁻⁷. Many of the histone kinases studied are stimulated by cyclic AMP^{6,8}.

In examining nuclear extracts of Walker-256 carcinosarcoma for histone kinases we have found that such extracts supplemented with whole calf thymus histones and γ - ^{32}P -ATP yield a ratio of acid-labile to acid-stable protein phosphates from 2 to 3.5, dependent on pH. Further, we have found that histones I and IV are phosphorylated to produce acid-labile phosphates by at least two separate enzymes obtained from Walker-256 carcinosarcoma nuclear extracts and similar extracts of normal rat tissues. The new kinases are apparently independent of cyclic AMP.

The new histone kinases were assayed in an incubation volume of 0.2 ml, containing: glycine-NaOH buffer (pH 9.5), 10 μmol , or maleate buffer (pH 6.5), 10 μmol ; γ - ^{32}P -ATP, 0.03 μmol , containing about 1.5×10^6 c.p.m.; magnesium acetate, 4 μmol ; ethylene glycol bis-(β -aminoethyl ether)-N,N'-tetraacetic acid, 0.03 μmol ; and histone IV or histone I, 20 μg . The reactions were started by addition of enzyme, and incubations were carried out for 5 min at 30° C. The reactions were terminated by the addition of 88% phenol buffered with 0.01 M sodium phosphate to pH 8, and the acid-labile ^{32}P bound to protein was determined by the phenol extraction-acetone precipitation method of Boyer and Bieber⁹.

Nuclei from all tissues studied except brain and regenerated rat liver were prepared by the method of Chauveau *et al.*¹⁰ except that $MgCl_2$ was used in place of $CaCl_2$. Brain nuclei were prepared by the method of Lovtrup-Rein and McEwen¹¹, and regenerated rat liver nuclei were prepared by the method of Higgins and Anderson¹².

Crude extracts from the Walker-256 carcinosarcoma nuclei, when assayed for the formation of acid-labile histone phosphates, showed a bimodal pH profile with one peak of activity at pH 9.5 (the 'pH 9.5 kinase') and another peak of activity at pH 6.5 (the 'pH 6.5 kinase'). Nuclei from rat spleen and from regenerated rat liver had activities similar to those of Walker-256 carcinosarcoma (Fig. 1a), while nuclei obtained from rat liver and from rat brain had only the pH 6.5 activity (Fig. 1b). Kidney nuclei have an apparently unique enzyme with a pH optimum about 8.7 (Fig. 1b).

The new histone kinases are principally found in the acidic protein fraction prepared from nuclei by the method of Wang¹³ and have been further purified from this fraction by isoelectric precipitation and chromatography on carboxymethyl cellulose. The pH 6.5 kinase washes through the carboxymethyl cellulose column, while the pH 9.5 kinase is eluted by 0.2 M NaCl, 0.01 M Tris-HCl (pH 7.5).

Among the basic proteins examined, histone IV is phosphorylated most extensively, while histone IIB and protamine are slightly phosphorylated by the pH 9.5 kinase. Histone I, casein, bovine serum albumin, poly-L-lysine, and poly-L-arginine are only poorly or not at all phosphorylated (Fig. 2a). The pH 6.5 kinase most extensively phosphorylates histone I, while histone IV is phosphorylated to a lesser extent (Fig. 2b). The pH 9.5 and pH 6.5 kinases are further distinguishable from one another with respect to their kinetics of phosphate incorporation, which may be related to the behaviour of histone IV in solution at pH 9.5.

When ^3H -histone IV (isolated by the Johns method¹⁴ from Walker-256 carcinosarcoma cells grown in tissue culture in medium containing ^3H -arginine) was phosphorylated using the pH 9.5 kinase and isolated by electrophoresis on cellulose acetate¹⁵ for 15 min at 110 V, the electrophoretic mobility, as measured by the co-migration of the ^3H and the ^{32}P labels toward the anode, was altered significantly from that of unphosphorylated ^3H -histone IV. The latter migrates very slowly toward the cathode under these conditions. Analogous studies using ^3H -histone I and the pH 6.5 kinase resulted in a similar alteration in the mobility of histone I. Dephosphorylation of histone I phosphate yielded free ^{32}P -phosphate and intact histone I.

Hydrolysis in 3 M KOH of the ^{32}P -labelled histone IV result-

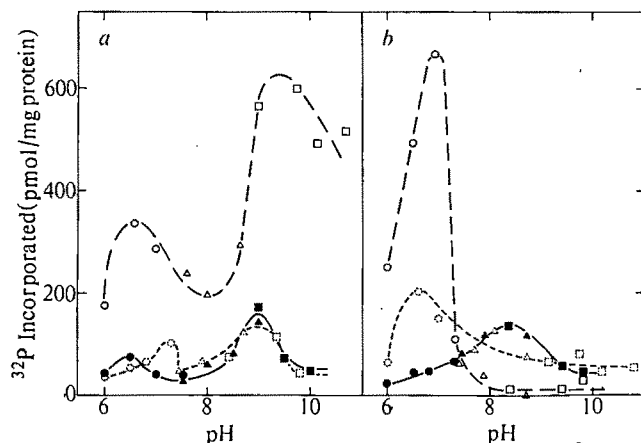


Fig. 1 Acid-labile histone phosphate produced as a function of pH using nuclear extracts: a: —, Walker-256 carcinosarcoma; ---, rat spleen; —, regenerated rat liver. b: —, rat brain; ---, rat liver; —, rat kidney. Buffers used were: ○, ○, or ●, phosphate (Walker-256 carcinosarcoma and rat liver) or maleate (other tissues); △, △, or ▲, Tris-HCl; □, □, or ■, glycine-NaOH.

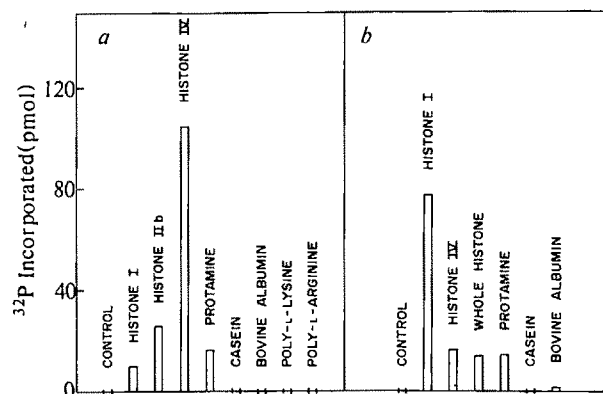


Fig. 2 Substrate specificity of the partially purified histone kinases. a, pH 9.5 kinase; b, pH 6.5 kinase. 20 μ g of the specified protein was added to the reaction mixture for each determination and assays performed as outlined in the text.

ing from the pH 9.5 kinase and subsequent paper chromatography of the hydrolysate in *n*-propanol:ethanol: $H_2O:NH_3$ (30:30:39:1) yielded ^{32}P -3-phosphohistidine. This observation has been confirmed by coupled Pronase-trypsin digestion of the phosphorylated histone IV. Studies on the chemistry of the phosphorylated lysine-rich histone produced by the pH 6.5 kinase reaction are in progress.

Our study shows the existence of at least two previously undiscovered nuclear histone kinases which catalyse the formation of acid-labile histone phosphates. Previously, the only known histone phosphates contained acid-stable phosphomonoester linkages. The two histone kinases we have found are distinguishable from one another with respect to various criteria, including the optimum pH for activity and the type of histone phosphorylated.

It is generally believed that phosphorylation of histones results in a loosening of the interaction between histones and DNA so that transcription or replication can occur. The temporal relationship of the new histone kinases to DNA synthesis and other cell cycle events is being studied with synchronised Walker-256 carcinosarcoma cells in culture.

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Elevated Erythrocyte Calcium in Sick Cell Disease

CUMULATIVE membrane damage and loss is thought to occur in the erythrocytes of individuals homozygous for haemoglobin S (refs 1-4). The culmination of this process seems to be the formation of irreversibly sickled cells (ISC), which will not resume normal biconcave disk shape, even when the haemoglobin which they contain is in the sol (oxygenated) state⁵⁻⁷. Although the processes responsible for the formation of ISC have not yet been fully elucidated, it is clear that a change in the structure or composition of the membrane has occurred, such that cellular plasticity and ability to resume normal shape upon oxygenation have been lost. Weed *et al.*⁸ report a similar loss of plasticity, a diminished ease of ingress into glass microcapillaries, when calcium is placed inside resealed membrane "ghosts" made from normal human erythrocytes. In whole red cells, diminished filterability was also found to occur concomitantly with progressive loss of ATP. ATP-depleted red cells, however, retained most of their plasticity if EDTA were added to the incubation mixture to prevent calcium accumulation⁸. These results indicate that increased calcium alone may markedly reduce red cell plasticity.

From this evidence, and the fact that sickle cells, especially in the deoxygenated, sickled state, are excessively permeable to cations such as sodium and potassium⁹⁻¹¹, we postulated that increased intra-erythrocytic calcium concentrations might occur in Hb SS disease. This accumulation of calcium within the red cell might lead to diminished filterability, and, eventually, to the formation of ISC. The results reported here support this hypothesis.

Erythrocytes from heparinized blood samples were washed four times in phosphate buffered glucose saline (pH 7.40, 10 mM dextrose) before quantitative analysis of red cell calcium concentration. This was carried out by atomic absorption spectroscopy according to the techniques reported by Weed *et al.*³ except that only one trichloroacetic acid (TCA) extract was made, one volume of thoroughly washed red cells being precipitated with five volumes of cold 10% TCA with 20,000 p.p.m. lanthanum. Quantitative recovery using this extraction technique was confirmed by counting extracts of erythrocytes which had been previously equilibrated with $^{45}\text{Ca}^{2+}$. Scanning electron microscopy and energy dispersive X-ray spectroscopy were performed on erythrocytes mounted on glass cover slips, fixed in 1% glutaraldehyde and subsequently washed in calcium-free isotonic dextrose to remove surface salt contamination. Individual ISC, defined as erythrocytes deviating markedly from biconcave disk shape, and sickle erythrocytes of normal morphology were found using scanning electron microscopy (Kent-Cambridge Stereoscan microscope). Energy dispersive X-ray spectroscopy¹² was used to analyse these individual cells for calcium. This technique involves exposing portions of individual cells to an electron source and measuring the resultant dispersed energy arising from individual elements within the cell. Because this technique does not allow absolute quantitative analysis, calcium was expressed as the ratio of calcium counts to aluminium counts. The aluminium counts were simultaneously obtained from the collector face of a beryllium-windowed 'Kevex' X-ray detector. Calcium flux studies were performed using washed packed red cells suspended to 30% by volume in Krebs-Ringer bicarbonate, containing 10 mM dextrose, 2.5 mM CaCl_2 , and 5.0 $\mu\text{Ci ml}^{-1}$ $^{45}\text{Ca}^{2+}$. After incubation with labelled calcium, the red cells were thoroughly washed at 4° C to remove all external calcium, extracted with five volumes of 6.7% TCA and the residual radioactivity was counted. In all procedures, as many white cells as possible were removed.

Quantitative analysis of erythrocyte calcium by atomic absorption spectroscopy revealed that Hb SS erythrocytes contained approximately eight times more calcium than erythrocytes from normal controls (Table 1). Furthermore,

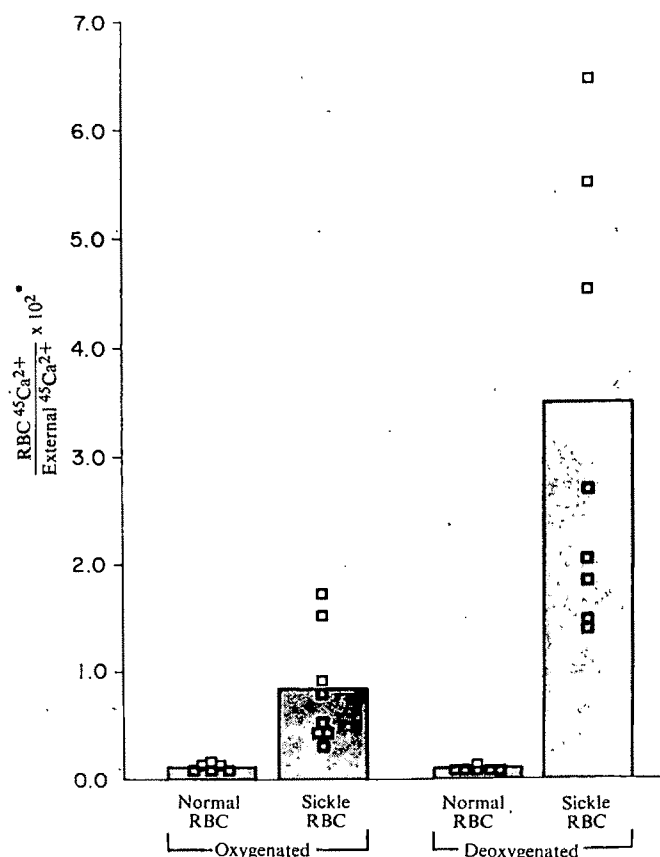


Fig. 1 Calcium leak into oxygenated and deoxygenated normal and sickle erythrocytes expressed as % of external $^{45}\text{Ca}^{2+}$ entering the red cells during 1.5 h incubation in a shaking water bath at 37° C. Samples of washed red cells were equilibrated in a tonometer with either 95% O_2 and 5% CO_2 or 95% N_2 and 5% CO_2 . □, Individual values. Means for each group are represented by the bars. Means (±1 s.d.) are as follows: oxygenated normal RBC, 0.072 ± 0.028 ; oxygenated sickle RBC, 0.840 ± 0.572 ; deoxygenated normal RBC, 0.090 ± 0.035 ; deoxygenated sickle RBC, 3.490 ± 1.884 . Significance of differences (Student's *t* test, two tailed): between oxygenated normal and sickle RBC, $t=3.177$, $P<0.01$; between deoxygenated normal and sickle RBC, $t=4.398$, $P<0.001$; between oxygenated and deoxygenated sickle RBC, $t=3.808$, $P<0.01$.

energy dispersive X-ray spectroscopy of individual Hb SS erythrocytes showed that, within the same preparation of well-oxygenated red cells, those which were "irreversibly sickled" contained approximately twice as much calcium as red cells of normal morphology. The ratio of calcium to aluminium averaged 3.01×10^{-3} (± 0.68) in eight ISC compared to 1.52×10^{-3} (± 0.04) in five sickle red cells of normal morphology ($t=4.839$, $P<0.001$).

To determine the origin of the greatly increased calcium concentrations, the influx of $^{45}\text{Ca}^{2+}$ into Hb SS red cells was measured. When washed red cells were incubated in Krebs-Ringer bicarbonate buffer with $^{45}\text{Ca}^{2+}$, the net influx of calcium into fully oxygenated Hb SS red cells was almost ten times that into normal red cells (Fig. 1). Furthermore, when oxygenated and deoxygenated (sickled) Hb SS erythrocytes were compared, it was found that calcium flux was enhanced

Table 1 Erythrocyte Calcium Concentrations in Normal Subjects and Patients with Haemoglobin SS Disease

Subjects	n	Mean	Range
Normal	14	24.9 (±8.2)	15.5-38.9
Hb SS disease	9	188.8 (±68.8)*	111.0-302.3

Values are expressed in $\mu\text{mol Ca}^{2+} \text{ l}^{-1}$ packed red cells ± 1 s.d.
* $t=8.824$, $P<0.001$ (Student's *t* test, two tailed).

more than four-fold by the sickling of Hb SS red cells. In contrast, deoxygenation had no effect on calcium leak into normal red cells. Control studies on samples from patients with elevated (>7%) reticulocyte counts revealed normal calcium flux rates (data not shown). Most of the uptake of $^{45}\text{Ca}^{2+}$ by sickle red cells probably represents exchange of unlabelled intracellular calcium for labelled extracellular calcium but three samples of deoxygenated Hb SS red cells, incubated for 1.5 h at 37° C, were found to accumulate an average of 50 μM Ca^{2+} l^{-1} of packed cells. No net accumulation was detectable in three control samples from normal individuals. This calcium accumulation in Hb SS erythrocytes was equivalent to a 25% increase in total cellular calcium.

We have found that Hb SS erythrocytes contain approximately eight times as much calcium as do erythrocytes from normal individuals, that ISC appear to contain approximately twice as much calcium as do Hb SS cells of normal morphology and that Hb SS red cells display markedly increased permeability to calcium, which is further enhanced by deoxygenation and sickling of these erythrocytes. This evidence indicates that the leakiness of Hb SS red cells leads to an abnormal accumulation of intracellular calcium. This, perhaps combined with progressive metabolic depletion, could explain the diminished filterability of oxygenated Hb SS red cells which has been reported by several investigators¹³⁻¹⁶, and is likely to be critically involved in the shortened survival of Hb SS red cells. LaCelle *et al.*¹⁷ have proposed that increased calcium and decreased ATP concentrations cause the stiffening of the erythrocyte membrane which characterizes normal senescent red cells. Membrane stiffening, in turn, would lead to sequestration and destruction of erythrocytes in reticuloendothelial organs such as the spleen and liver. A similar, though much more rapid, series of events seems to underlie the greatly accelerated red cell destruction in haemoglobin SS disease. In addition, marked calcium accumulation may be involved in the formation of ISC *in vivo*.

We suggest, as have others⁸, that calcium alters the sol-gel characteristics of the red blood cell membrane, favouring the latter. In Hb SS erythrocytes, an excessive accumulation of membrane calcium, occurring during sickling, probably "fixes" the membrane in the sickled shape, thereby producing the ISC.

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Erratum

In the article "Accumulation of Fossil CO₂ in the Atmosphere and the Sea" by A. W. Fairhall (*Nature*, **245**, 20; 1973), Figs 1 and 2 of the original manuscript were substituted for the corresponding figures of the revised version. As far as Fig. 2 is concerned, the differences are small, but Fig. 1 (revised) contained data which were essential to the discussion. The correct figure appears below. Also line 2 of page 22 should read, " $[n_a' - n_a]/[N_a + n_a(t)]$ ", expressed as a percentage where $t' =$ ".

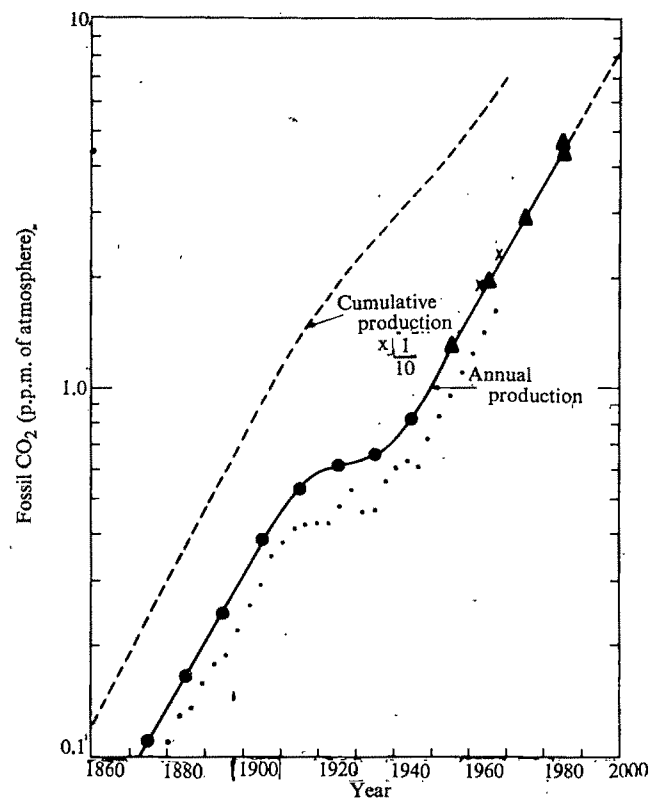


Fig. 1 Production of fossil CO₂ since the 1870s: the solid circles are the estimates of Revelle and Suess¹⁰ extended to 1890 by estimates of OECD, which along with the data from the 1960s are from ref. 11. The dots are estimates of Keeling¹². The dashed line is the cumulative production to the present day based on the Revelle-Suess production curve.

The author also wishes to take this opportunity to add the following information:

Using a simple box model for the atmosphere, biosphere, mixed layer of the sea, and the deep sea, and a logistic-curve representation of future fossil CO₂ emissions, Zimen and Altenheim^{1,2} have reached substantially the same conclusions as myself. In their analysis the calcite undersaturation of the sea would be reached before the turn of the century.

- ¹ Zimen, K. E., and Altenheim, F. K., *Naturwissenschaften*, **4**, 198 (1973).
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BOOK REVIEWS

Plants People Ate

Palaeoethnobotany: The Prehistoric Food Plants of the Near East and Europe. By Jane M. Renfrew. Pp. xvii+248 (48 plates). (Methuen: London, May 1973.) £6.50.

DR RENFREW begins this attractively produced book with a definition of palaeoethnobotany: "the study of the remains of plants, cultivated or utilised by man in ancient times, which have survived in archaeological contexts". She is concerned primarily with the palaeoethnobotany of the Near East and Europe in prehistoric times and with plants utilised for food rather than as sources of structural materials, textiles, dyes or medicaments. Her main intention is to bring together in a single volume the information available for the identification of archaeological plant material, for without accurate identification the results of palaeoethnobotanical investigations cannot be interpreted meaningfully. The book therefore describes and assesses the evidence from which it has proved possible to attempt a reconstruction of the history of man's plant foods during the past ten thousand years or so.

The initial chapter reviews the development of palaeoethnobotanical research since the pioneering publications of C. Kunth (1826) and Oswald Heer (1866), and pays just tribute to the long series of fundamentally important contributions by Hans Helbaek, of the National Museum in Copenhagen, whose establishment of principles and techniques for the identification of plant remains and especially of seeds, grains and fruits has placed all workers in this field deeply in his debt.

There follows a general survey of the evidence, the survival of which has been for the most part due to carbonisation by heat, continuous waterlogging in peat deposits or desiccation in desert sand but also to the accidental preservation of impressions of seeds and fruits in the wet clay of pottery before firing or, less frequently, in the mudbrick or daub of walls before sun-drying. With regard to the very large numbers of grains and seeds found carbonised, Dr Renfrew gives no support to the belief that this might be the result of spontaneous anaerobic processes taking place at normal temperatures but regards carbonisation as arising simply from overheating near a hearth or in a parching oven or sometimes from a house fire: she reminds us that the ears of hulled wheats require parching before they can be successfully threshed or winnowed. She, like many others, has

been concerned about the effect of carbonisation, or indeed of any mode of preservation, on the dimensions and shape of plant parts and she quotes the results of experiments, including her own, which enable estimates to be made of the extent of deformation in various circumstances. It is of interest that prehistoric grains must in most instances have been smaller than their counterparts of today.

Carbonised material may preserve a good deal more than the gross morphological features: "occasionally the surface . . . is so well preserved that it is possible to study the cell pattern and even the structure of the hairs". Helbaek has shown, too, that silica skeletons of epidermal cells of cereal grains and their glumes may persist even in impressions in mudbrick or baked clay, thus much increasing the possibilities of critical identification. It seems likely that the services of the scanning electron microscope will become increasingly valuable in future.

The palaeoethnobotanist seeks to answer such questions as what type of food economy was practised and, if there was crop agriculture, what were the crops, whether they were grown singly or in mixture and in what relative amounts. This demands not only the discovery of suitable sites but also the correct decisions as to how the plant remains are to be extracted and sampled. Dr Renfrew shows in a table of results from Tell Azmak in Bulgaria that the whole of the material in a single find may constitute too small a sample for any but very hazardous inferences: finds at contemporary levels in the same site have remains of from one to five plant species. Even where there is adequate material there are dangers of sampling bias from various causes, and the finds themselves are likely to be products of some degree of contemporary selection, so that interpretation must be doubly cautious. The whole topic is of the utmost importance and it could be argued that Dr Renfrew might have devoted even more space to it.

Chapters 4 to 16 describe the major temperate food plants of prehistoric sites, indicating the location and dating of their finds and explaining how they can be identified and differentiated from their closest relatives. There are many excellent line drawings by Alan Eade and some informative half-tone plates at the back of the book. There are also numerous tables of characters and measurements, so that palaeoethnobotanists should be greatly assisted in solving problems of identification.

Chapter 20 considers the food values of prehistoric plant foods, but it is difficult to infer more than that the foods included important sources of carbohydrates, fats and proteins and that various fruits were probably eaten fresh: green foods would not have been preserved. The final chapter is a brief review of the origins and development of crop agriculture in the Near East and its spread to Europe. Dr Renfrew's own investigations in Europe give great weight to her views on this topic. She accepts that the first farmers reached the Balkan Peninsula soon after 6000 bc and that they brought emmer wheat as the chief cereal crop, together with einkorn wheat, both two-row and six-row barleys, oats and various pulses. The naked club and bread wheats appear quite early in the neolithic, but spelt wheat and rye not before the late neolithic. Dr Renfrew is rightly content to present the archaeological facts and does not much concern herself with evolutionary theories based on cytogenetic findings. A much larger body of archaeological data seems necessary before workers should be worried by any failures of the two lines of approach to yield identical conclusions.

Dr Renfrew emphasises the antiquity and scale of the cultivation of leguminous crops. Peas, lentils and vetches found in the earliest farming sites may have been collected in part from wild plants, but the cultivation of pulses seems as old as that of cereals. Much of the general interest of this book lies in the information provided about food plants other than cereals and pulses. Thus acorns, pistachio nuts, cornelian cherries (*Cornus mas*) and crab apples occur in early neolithic farming sites in SE Europe, and figs, wild pears and wild grapes in Greece from the late neolithic onwards. Further north there is evidence for the collection or cultivation of cherries, bullaces, sloes, raspberries, blackberries, haws, whitebeam fruits, rose hips, elderberries, bilberries and water chestnuts (*Trapa natans*). Besides acorns there are almonds, walnuts, hazelnuts and beech-nuts; and there are the numerous weed seeds which are known to have been collected, some more and some less intentionally, and eaten in bread or porridge. The whole list is interesting and impressive as illustrating the large-scale persistence of food collecting into the agricultural period.

There are a few misprints and a few obscurities, and Helbaek's 1963 publication, cited on pages 9 and 11, does not appear in the bibliography. These are small matters. Dr Renfrew must be

congratulated on having achieved her aim of providing for palaeoethnobotanists a much more comprehensive and systematic guide to the identification of plant remains than has been available until now and, moreover, of providing at the same time a very welcome source book of information for the general scientific reader.

A. R. CLAPHAM

The Excitable Heart

Electrical Phenomena in the Heart. Edited by Walmar C. De Mello. Pp. xv+415. (Academic: New York and London, October 1972.) \$26.

New blood has kept the field of cardiac electrophysiology fertile and by drawing upon it Professor De Mello has ensured the success of his enterprise, although the absence of a preface is a pity. Those starting a career in cellular physiology and biophysics, and to whom the book is addressed, need to know how the editor views the subject as a whole: better to expose the logic or hunch by which the chapters have been strung together than to imply questionable connexions by tacit juxtaposition.

The volume opens with "Electrical Properties of Embryonic Heart Cells" by N. Sperelakis. From the biological point of view this is a rational beginning, but since familiarity with the electrophysiology of the adult tissue is required for the appreciation of this informative article, some readers will find W. K. Berger's chapter on "Ultrastructure and Function of Cellular Contacts" an easier starting point. The morphology of cardiac muscle and the mechanism of excitation spread are well reviewed therein. H. Fozzard's lucid article on membrane capacity of cardiac muscle cells, out of place as chapter 8, might well be read next since structural considerations enter closely into the interpretation of the measurements.

The task of exposing the nature of the cardiac action potential is shared out between J. Dudel who deals mainly with the fast excitation process, and D. Noble and R. W. Tsien who cover the events during the plateau phase in a helpfully interpretative way. The generation of action potentials in spontaneously beating Purkinje and auricle fibres is touched upon briefly by both Dudel and Noble and Tsien. The reader pursuing the leads to voltage-clamp experiments given in their articles will find that the pacemaker potential can also be ascribed to voltage and time-dependent conductance changes controlling the downhill flow of ions. Quite a different hypothesis is advanced by T. C. West who, in writing on "The Electrophysiology of the Sinoatrial Node", holds the main brief to deal with cardiac autorhythmicity. On the basis

mainly of the high temperature coefficient of the heart rate, he implicates active inward transport of potassium ions in the fall of K permeability during the diastolic interval. As an alternative hypothesis this may well require consideration, but it is puzzling why the voltage-clamp experiments bearing on the problem of autorhythmicity have been totally ignored. Presumably the editor was left to turn diverse views to constructive ends; but in the event this task falls upon the reader. From the touchlines the editor does, however, bias the issue by setting H. G. Haas's article on "Active Ion Transport" immediately before that on the sinoatrial node, as if the consideration of active transport were an essential preliminary to the problem of autorhythmicity.

Taken by itself the chapter on active transport makes rewarding reading. The emphasis placed on the great sensitivity of the cardiac action potential to variations in the metabolic state of the cells is well placed as this remains a pressing problem. The case for the participation of metabolically driven currents in shaping the action potential is, however, not compelling. A less direct mechanism, say a change in the intracellular concentration of an ion determining a surface potential on the inner face of the excitable membrane, could equally well be at work.

Under the title "Cardiac Innervation and Synaptic Transmission" M. Anderson and J. del Castillo cover the recent revival of histological research into the rich innervation of the specialized regions of the heart. The high chemosensitivity of natural pacemaker fibres permitted some time ago the demonstration of the mode of action of acetylcholine. The more recent work on the inotropic action of adrenaline is well summarized, but the treatment of the chronotropic action suffers from the inadequate cover given earlier in the book to the known kinetics of the pacemaker current.

From a perceptive chapter on atrioventricular transmission by C. Mendez and G. R. Moe it becomes clear that the slow inward current system plays an important part in the propagation of excitation through the node. At this point one misses in this otherwise laudable multinational book a contribution from one of the French laboratories where the slow inward current system has been explored.

After interesting chapters on "Comparative Aspects of Electrogenesis" by F. V. McCann and on "The Healing-Over Process" by W. C. De Mello the volume is rounded off with a comprehensive article on "Calcium Movements and Excitation-Contraction Coupling" by J. B. Bassingthwaite and H. Reuter.

O. F. HUTTER

Feeding Children

Malnutrition and Retarded Human Development. By S. L. Manocha. Pp. xv+382. (Charles C. Thomas: Springfield, Illinois, September 1972.) \$19.75.

We have known since the early years of this century that good nutrition has something to do with physical and mental development, and in many countries practical schemes to feed growing children as well as possible have been introduced. During the past twenty years or so during which international concern over the world food situation has intensified there has been increasing effort to solve questions relating to the nutritional needs of children, with the general aim that children everywhere shall be adequately nourished.

Many scientific problems remain to be solved, but much is now known about the nutritional needs of children and how to meet them, and Dr Manocha has done a useful service in assembling so much material in this review. His book, which is intended for the educated layman as well as the professional reader, is clearly and simply written. He discusses the biochemistry and physiology of human development, particularly of the brain, environmental influences, including socio-economic factors, maternal nutrition and food habits, and such practical matters as government schemes to alleviate malnutrition, guidance on the direction and treatment of the diseases of protein-energy malnutrition, and nutrition education.

Dr Manocha writes from an international point of view and shows by the number and variety of the references he cites that he has crossed national boundaries and brought together relevant material from established and active workers in all continents. Each of the nine chapters of the work ends with a list of authoritative references ranging in time from the early years of international anxiety about malnutrition in children to 1971. These lists would by themselves be invaluable to any student of nutrition.

One could point to minor errors in the names of certain authors and to the omission of ideas that appear to be becoming of crucial importance, such as how the overriding socio-economic problems of modern society are to be solved if proper physical and mental development is ever to be achieved for all human beings. But to do this would be to carp. This book can be recommended as a useful, comprehensive, simply written review of an important and topical subject. It could be read with profit by anyone who wishes to understand more about one of the most intractable subjects of our age.

D. F. HOLLINGSWORTH

Brown on Boranes

Boranes in Organic Chemistry. By Herbert C. Brown. Pp. xiv+462. (Cornell University: New York, August 1972.) \$24.50.

THIS book is part of a distinguished series in which eminent chemists have provided written records of their Baker Lectures at Cornell University. Professor Brown essentially gives a scientific autobiography. In this sense the title of the book is misleading in that the subject of organoboranes forms but one of six parts discussing various aspects of borane chemistry.

In part 1 the principal topics relate to diborane and borohydrides, and free radical substitution reactions. These two diverse topics commanded Professor Brown's interest because of the presence at the University of Chicago of H. I. Schlesinger and M. S. Karasch.

Part 2 is devoted to Brown's contribution to the assessment of the role of steric strains in chemistry. His work on donor-acceptor addition complexes of boron led him to the idea of these as models for saturated carbon compounds—strained homomorphs and the classification of steric strains (F-, B-, I-strains).

The non-classical ion problem, which is the topic of part 3, has been the subject of long-standing controversy, particularly with the late Saul Winstein, and has now become a part of chemical folklore. The relationship to the boron studies is perhaps based on the tenuous recognition that a carbonium ion is iso-electronic with a borane.

Part 4 is concerned with selective reductions using hydrides or complex hydrides of boron and aluminium and the question of selectivity. Reagents such as disiamylborane are uniquely associated with Brown, not least in their nomenclature.

In part 5, which is devoted to hydroboration and essentially updates Brown's monograph on the subject of 1962, the author is mainly concerned with boron-carbon bond-making. The term "hydroboration" is probably interpreted by the organic chemist as a combination of this process together with a subsequent boron-carbon bond-making, usually without isolation of the boron intermediate. The value of the overall procedure lies in a combination of factors which includes mild reaction conditions, essentially quantitative yields, a high degree of selectivity and stereospecificity, and a multiplicity of similar specific cleavage reactions. Thus it is possible to convert acetylenes or olefins to numerous functional derivatives including higher homologues. Part 6 deals with organoboranes from the point of view of boron-carbon cleavage reactions. From the standpoint of the

organic chemist, parts 5 and 6 thus form a continuous story.

Professor Brown is, and has been, one of the giants of chemistry of the last thirty years. He is a splendid controversialist, both verbally and in writing, and the present contribution is in this same happy tradition. M. F. LAPPERT

Structures in Cells

The Generation of Subcellular Structures. By R. Markham, J. B. Bancroft, D. R. Davies, D. A. Hopwood and R. W. Horne. Pp. x+372. (North-Holland: Amsterdam and London; Elsevier: New York, 1973.) Dfl 45; £7.

THE three-dimensional structures of subcellular biological systems and mechanisms for their biosynthesis are now elements of perhaps the most important next stage in molecular biology. The problem is ripe for attack and the timing and choice of this subject for the first John Innes Symposium (held in July 1972) could not have been more appropriate. It has been excellently organized and the individual subsections well selected, being here presented in a series of stimulating articles by leading exponents from many parts of the world.

Prefaced by a suitably general historical review of molecular genetics in the form of the sixth Bateson Memorial Lectures by W. Hayes, the proceedings of the meeting include a fairly wide collection of original reports on the structure and synthesis of organelles (usually in the form of summaries of recent advances). The range stretches from relatively simple systems such as bacterial flagella and plant viruses through larger viruses, such as T₄ phage, towards bacterial spores and the more complex sophistications of ribosomes, cell walls and mitochondria. Contributors include D. Kerridge, H. R. Revel, E. Kellenberger, J. G. Atabekov, M. Nomura, R. A. Cox, A. Ryter, P. C. Fitzjames, Audrey Glauert, B. A. Afzelius and many others.

It is worth noting that all the systems considered here derive from viruses or prokaryotes, where the relatively simple structures involved are easier to study than the complexities of eukaryotes, but where the basic lessons to be learnt and the models that emerge are applicable to all types of living systems.

Perhaps the most fundamental problem in this field is the extent to which all necessary information for the correct assembly of subcellular organelles (indeed for the whole cell, for that matter) is contained in the structures of their constituent molecules. Another (slightly more restricted) way of putting it would be to ask whether the DNA or RNA genome contains all the necessary instructions for putting together the nor-

mal three-dimensional structures involved. This naturally leads to two rather more specific queries. (1) How far can assembly of multimolecular complexes occur in the absence of pre-existing structure and, in cases where some sort of pre-existing structure is required, how specific must it be? (2) To what extent, in the construction of such complexes, is a sort of scaffolding necessary—in the sense of an essential structure that is not contained in the final finished organelle?

The articles in this symposium do not of course provide a complete, generalized answer to this sort of question. But they begin to indicate the sorts of ways in which answers can be given. It would be impossible to summarize any general conclusions, although the reader is left with a strong feeling that this is an area where much progress will occur rapidly during the next 10 years.

Perhaps, above all, what has emerged fairly clearly is the extent to which spontaneous assembly of relatively complex structures can occur (being often demonstrable *in vitro*) simply through molecules "finding each other" by interactions between complementary patterns on their surfaces. Temporary scaffolding, specific catalysis by enzymes, complex "foundation" molecules acting as a specific nidus for the association of other key molecules—if they exist (as they appear to do in certain cases)—are not always necessary, although there is often an obligatory sequence in the assembly process (for example, with ribosomes) and/or a polarity in the direction of build-up, even of monomers in simple complexes such as flagellar filaments.

Having emphasized what a fascinating collection of articles is here available in an exciting field, some protest must be made about the publication itself. The offset-type process used is more tiring and difficult to read than ordinary print, the legends are not properly distinguished from the text, some tables are in type almost too small to decipher, the section headings do not stand out clearly and italics are not properly visible. The discomfort involved might be tolerable if the book were cheap.

M. R. POLLOCK

Practical Concern

Guide for Safety in the Chemical Laboratory. Second edition. (Manufacturing Chemists Association.) Pp. vi+505. (Van Nostrand Reinhold: New York and London, 1972.) £8.75.

A SMALL stretch of the imagination should inform us that the first task of the contemporary, socially concerned scientist is to make sure that neither he nor those working with him are blown up, burnt to cinders or dissolved in acid. Yet it is a matter of record

that very few institutions of higher learning are giving their students anything but the most cursory advice in laboratory safety and accident prevention on the time honoured basis that God, somehow, will couple the shorn lamb with the careless chemist. Industry, whose managers tend to be better informed on the hard realities of economic loss and the trade unions' inclination to fight compensation suits, is understandably more advanced.

In this situation it is always pleasant to welcome a new book which advocates more thought in the design and manning procedures of laboratories. Such publications come in two types: one, for example the *Handbook of Laboratory Hazards*, now published by The Chemical Society, lays emphasis on what to do once the accident has occurred and notes those chemicals with which potential danger is always present. The volume under review, produced by the American Manufacturing Chemists Association, takes a step back and considers safety as a logical outcome of sensible design and behaviour. Except in the most general sense it is not suitable as a quick reference volume in moments of stress: although it abounds in tables, so it does in cross references which take some time to follow through. But as background reading it is most valuable, for it takes nothing for granted and leads the teacher or laboratory supervisor step by well illustrated step through all the pitfalls of space, instruments and chemicals—when did you last test your fire extinguishers?

Frequently American practice differs from the British and there are variations in detail in regulations and materials standards: hence reference to ASTM. Nevertheless those whose work involves the manipulation of chemicals and the safety of the people concerned will derive great benefit from keeping *Guide for Safety* on their bookshelves, especially in the unlikely event that a fit of generosity from UGC, DES or head office allows them to translate dreams of a new laboratory into reality.

PETER FARAGO

Particle Physics

Elementary Processes at High Energy. ("Ettore Majorana" International Centre for Scientific Culture, 1970 International School of Subnuclear Physics, a NATO-MRI-MRST Advanced Study Institute sponsored by the Regional Sicilian Government and the Weizmann Institute of Science, Erice, July 1-19.) Edited by A. Zichichi. Part A. Pp. xix+1-448. Part B. Pp. xvii+449-861. (Academic: New York and London, April 1972.) \$29.50 each part.

THIS two-volume record of the 1970 International School of Subnuclear

Physics held at the hill-top town of Erice in Sicily, is a welcome addition to the scientific literature on elementary particle physics. It maintains a very high standard, and contains many lectures and discussions with permanent value.

Volume A contains the lecture courses and the review lectures, the relevant discussions being collected to follow each set. The lecture courses were of course quite topical. The opening lecture, "Electron-positron annihilation", by N. Cabibbo, was especially timely, in view of the recent operation of the electron-positron storage ring ADONE at Frascati and the early experimental results reported at the School by Italian groups working with ADONE.

G. Veneziano contributed an outstanding set of lectures about narrow resonance models compatible with duality. Besides his illuminating discussion of the origination of the model, he described clearly its generalisation to the N-point functions which many authors have discussed for scalar particles in the literature. T. D. Lee lectured on the Lee-Wick formulation of quantum electrodynamics, which makes use of an indefinite metric; his lectures included a critical analysis of the notion of causality, as used in elementary particle physics. H. Harari presented the qualitatively successful picture of hadron reaction processes which has resulted from an amalgamation of the duality model, the absorption model, and the quark model. Here his lectures are compressed into a novel but effective format, a picture book approach consisting of twenty-nine figures, self-explanatory to some extent but each with a figure caption, and a number of remarks added by way of introduction and conclusion. Whereas Harari's "picture book" occupies twenty-two pages, the discussion following them goes on for a further thirty-four pages.

Two review lectures on gravitational topics were given by W. Thirring from an elementary particle physicist's viewpoint, "more than a sort of exercise in Riemann geometry for esoteric theoreticians; something more down to earth". His second lecture "A trip behind the Schwarzschild radius", would, perhaps, be entitled today "Inside a black hole". Once considered outside elementary particle physics, gravitational topics are now attracting and intriguing many people in this field. Two review lectures were also contributed by T. D. Lee, the first an interesting introduction to symmetry principles in physics, and the second a critical discussion of published derivations of the $\Delta I = 1/2$ rule from soft pion theorems. Coming from Frascati, G. Salvini surveyed the status of experiments on electron-positron storage rings which bear on quantum electrodynamics, on the vector dominance model for photon interactions and on searches for new vector mesons. Finally, B. Maglic reviewed the problems of meson spectroscopy, including his proposal to study $\pi-\pi$ and $\mu-\mu$ collisions at low energy, using the self-colliding orbits of his "Preceptron" device.

The seminar talks are collected together in volume B, and cover a wide range of topics, not all of which can be mentioned here. J. Adams recounted the possibilities considered for the super-CERN accelerator. His words are interesting to read today, and make us realise how wise was the final decision, in relation to the boundary conditions which existed at that time. V. Weisskopf contributed an instructive seminar about nucleon structure, as seen in the light of the scaling law now established for inelastic scattering. The study of $\pi\pi$, $K\pi$, and $K\bar{K}$ interactions was covered thoroughly in an extensive series of seminars by P. Schlein. Especially appropriate at this School were the seminars contributed by M. Conversi and by A. Zichichi, concerning the work in progress by their groups at ADONE.

Many other seminars with much topical interest were also given, about the light-cone behaviour in quantum field theory, and its application to lepton-pair production, about vector meson dominance and deep inelastic electron-proton scattering, about the Pomeranchuk theorem and the possible ways in which it may fail, about SU(4) symmetry and its merits with respect to weak and strong interactions, and about PCAC, among other topics. One topic unusual for such a school was that discussed by U. Amaldi, the developments in nuclear physics which have been achieved by using high-energy particles produced by energetic accelerators. He described particularly how the analysis of quasi-free collisions, processes of the type (p,2p), has provided our strongest evidence for the validity of shell-model wave functions for light nuclei. The closing lecture, an interesting and authoritative history of the development of our knowledge of the properties of the weak decay interactions, was given by T. D. Lee.

The extensive discussion after each lecture has been an outstanding feature of the Erice School, and this has been recorded in full in these volumes. The audience included many students at the postdoctoral level, as well as many senior visitors who were there to lecture or to give seminars. Consequently, this discussion was at quite a high level, and frequently very illuminating. The record of these discussions is one of the most valuable aspects of this book.

R. H. DALITZ

CORRESPONDENCE

CO₂ Pollution of the Sea

SIR,—A recent communication (*Nature*, 245, 20; 1973) suggested that a slight increase in partial pressure of CO₂ would shift the HCO₃ equilibrium system far enough to prevent secretion of shells in marine corals and molluscs.

The lower carboniferous shells were secreted when the partial pressure of CO₂ was more than 300 times current levels (before the carbon of the coal measures was produced by species which themselves required high partial pressures of CO₂ to grow so luxuriantly).

The two statements are incompatible although the chemistry seems equally valid in both cases. However, I have never seen a systematic approach to palaeoatmospheric analysis and have long wondered at the ability of species to proliferate in spite of using an oxygen combustion system, in an atmosphere rich in CO₂, with primitive respiratory systems and inefficient internal oxygen transport arrangements. Popular assumptions about the primitive atmosphere may be wrong, otherwise ethologists have problems they have neglected.

Yours faithfully,

G. A. WOOD

13 Clifton Park Road,
Davenport Park,
Stockport

Are Conferences Necessary?

SIR,—As a means of communication of scientific data and theory, are conferences worth the money and effort being spent on them? Many think not, but

before such established and prestigious activity can be changed it is scientifically proper that experiments should be done.

Recently an attempt was made to break the established pattern by having a meeting based on the following concepts: (1) that satisfactory communication can only be achieved if the participants are limited to those actively engaged in relevant experimental work and who can sit around one, albeit large conference table; (2) that this close interaction between participants be maintained away from the conference table; (3) that participants should arrive knowing in detail the topics to be discussed; (4) that experiments to resolve some of the controversial problems described in the papers should be made at the meeting; (5) that these experimental procedures should be able to be changed on-line at the suggestion of the participants.

The subject of the conference was "Event Related Slow Potentials of the Brain" and was concerned with the changes of the electroencephalogram associated with external stimuli and with voluntary and involuntary motor movements ranging from speech to spinal reflexes. Forty-five invitations were sent to active workers in the field. It was estimated that about 200 people would have attended an unrestricted conference. The meeting was held in a relatively inaccessible college in which most of the participants were accommodated. Most of the forty papers were precirculated and only discussion was allowed at the meeting. One and a half days were devoted to experiments performed in the research laboratory of this Institute and relayed by closed circuit television.

There was no mixing or editing of pictures from the four cameras as in normal television procedure; all cameras were on all the time and thus gave considerably more information than if the audience were in the laboratory. A television camera and microphone in the auditorium permitted participants to communicate with the demonstrators.

The demonstrations were separated into five sessions representing five aspects of the congress theme. They were presented by selected groups of participants with the help of the Institute staff. A total of 12 h television transmission was achieved.

There was good interaction between experimenters and audience and on occasions the experiments were modified to clear a particular point in dispute. These were experiments in the true sense of the word—procedures adopted on chance of their succeeding. All participants were enthusiastic about these experiments.

This format for conferences appears to be of considerable value in the presentation of data and organisers of meetings are urged to reconsider their objectives and methods and to carry out the necessary experiments.

Yours faithfully,

R. COOPER

Chairman, Organising Committee,
3rd International Congress on Event
Related Slow Potentials of the Brain,
and
Scientific Director,
Burden Neurological Institute,
Stapleton, Bristol

Obituary

A. G. Sharov

THE prominent insect palaeontologist Dr Alexander Grigorievitch Sharov died suddenly in Moscow on July 10, 1973.

Dr Sharov was born in 1922 in the village of Lukino, Moscow Region. While still a schoolboy he developed an interest in entomology, collecting insects and observing their habits and behaviour. After finishing school in 1939, he entered the Biological Faculty of Moscow University and specialised in entomology. While an undergraduate he took part in expeditions to the Far

East, Transcaucasia and Central Asia, where he collected material and made many interesting observations on the local faunas.

In 1943 Sharov was enlisted in the army and his military service lasted until the end of the war. He returned to Moscow University in 1945 and completed work for his diploma. In his student days, as in his later scientific work, Sharov was interested in the problems of insect ontogeny and evolution. His postgraduate studies began in the Institute of Evolutionary Morphology in Moscow, under the guidance of such prominent scientists as Pro-

fessors D. M. Phedotov and M. S. Ghilarov. In 1950 he was awarded a doctorate for his thesis on the 'proto-metabolous' development of the Thysanura and its bearing on insect phylogeny.

During the next few years Sharov's interests turned to fossil insects, and in 1955 he moved to the Palaeontological Institute of the Academy of Sciences of the USSR. There he worked until his death on the palaeontology, phylogeny and evolution of insects. He took part in many expeditions, collecting much remarkable fossil insect material. One of his most important discoveries was

that of the new order Monura, which he considered to be primitive ectotrophic Apterygota.

Sharov's works on the fossil insects of the Kuznetsky Basin are well known and highly regarded by insect palaeontologists. Most of his new discoveries were of Orthopteroid insects, and in 1968 he published a monograph on the phylogeny of this group. This comprehensive study, which was published in an English edition in 1971, will no doubt be the standard work on this subject for many years to come.

Sharov published a total of sixty-four papers and books. As well as a first-class scientist, he was a friendly and charming person, and his loss will be felt deeply by his many friends and colleagues.

Announcements

University News

Professor D. Samuel, Professor of Physical Chemistry, Weitzman Institute, has been appointed a Visiting Professor in the Department of Zoology and Comparative Anatomy, University College London.

Appointments

Dr J. W. B. King has been appointed director of the **Agricultural Research Council's Animal Breeding Research Organisation**.

Mr R. E. Boote has been appointed director of the **Nature Conservancy Council**.

The full membership of the **Computer Board for Universities and Research Councils** is now **Professor D. J. Finney**,

Professor A. J. Brown, **Mr A. H. Duncan**, **Professor J. C. Gunn**, **Dr J. Howlett**, **Professor K. W. Morton**, **Professor H. H. Rosenbrock** and **Professor M. Wells**.

Miscellaneous

Dr Basil Bard, Managing Director of the **National Research Development Corporation**, has been awarded the **Gold Medal** of the **Licensing Executives Society**.

Erratum

In the article "Comparison between Ice Age and Present General Circulations" by **E. B. Kraus** (*Nature*, **245**, 129; 1973), equation 1 should read $\theta_c = \theta_{exp}(rL/c_p T)$, and Table 1, line 4, should read $T_3(^{\circ}\text{C})$. Ref. 9 should also be changed to read **Bonatti, E., and Gardner, S.**, *Nature*, **244**, 563 (1973).

Corrigendum

In the article "Prostaglandin Production and Bone Resorption by Dental Cysts" by **M. Harris**, **M. V. Jenkins**, **A. Bennett** and **M. R. Wills** (*Nature*, **245**, 213; 1973), PGF_1 , PGF_2 and PGF_3 should read PGF_{1a} , PGF_{2a} , and PGF_{3a} throughout.

International Meetings

November 21, Symposium on Acylation (The Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London, SW1X 5AG).

December 5-6, Food Hygiene and the European Economic Community (Mr M. D. Ranken, BFMIRA, Leatherhead, Surrey).

December 6, Feeding the Newborn: Comparative Problems in Animals and

Man (Dr J. D. Sutton, National Institute in Dairying, Shinfield, Reading RG2 9AT).

December 6-7, Physical Properties of Solids at High Pressure (The Meetings Officer, The Institute of Physics, 47 Belgrave Square SW1X 8QX).

December 11, The Penetration of Liquids into Solids (The Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1X 8PS).

December 11, Teaching of Physics in Electronics Courses (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

December 14, Glaucoma Symposium (Office of the Director, The University of Texas Health Science Center at Houston, Division of Continuing Education, PO Box 20367, Houston, Texas 77025).

December 17-19, Computers in Spectroscopy (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

December 17-21, Congress on Marine Waste Disposal (Professor E. F. Frangipane, Institute of Sanitary Engineering, Milan Polytechnic, Piazza Leonardo de Vinci 32, 20133, Milan, Italy).

December 18, Recent Developments in Antibiotics (Dr J. F. Cavalla, John Wyeth and Brother Ltd, Huntercombe Lane South, Taplow, Maidenhead, Berks).

December 18-19, Polysaccharides: their Physical Chemistry and Molecular Biology (Dr D. A. Rees, Unilever Research, Port Sunlight, Cheshire).

December 26-31, American Association for the Advancement of Science Annual General Meeting (AAAS, 1515 Massachusetts Avenue, NW, Washington DC 20005).

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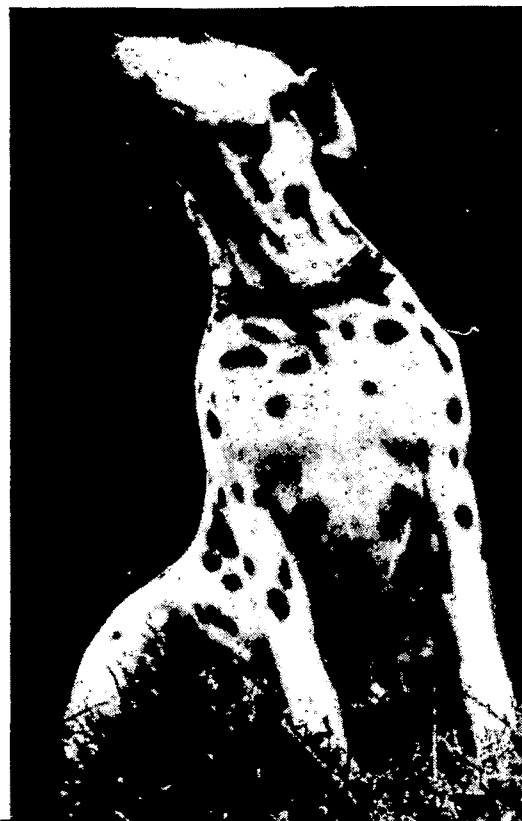
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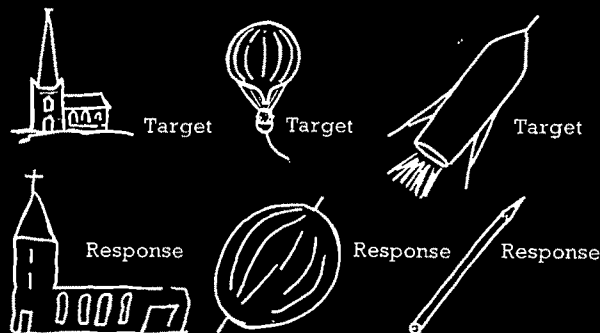
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Studies on cytology and differentiation in Sciaridae. 5. Electron microscopic studies on the salivary glands of *Bradysia elegans* Morgante (Diptera, Sciaridae). A. B. Da Cunha, R. W. Reiss, C. Pavan, J. J. Bieseke, J. S. Morgante and M. C. Garrido.

The principle of sequential dependence in cellular differentiation. P. A. Riley.

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The enrichment of egg-type RNA in cleavage stage embryos of the sand dollar *Dendraster excentricus*. Shigeki Mizuno, H. R. Whiteley and A. H. Whiteley.

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Neurite extension by mouse neuroblast: evidence for two modes of induction. P. Furmanski.

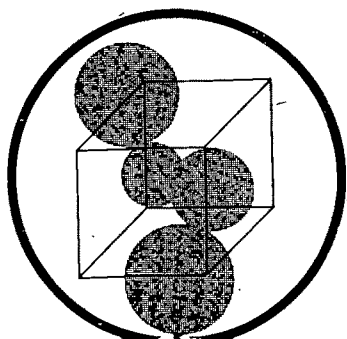
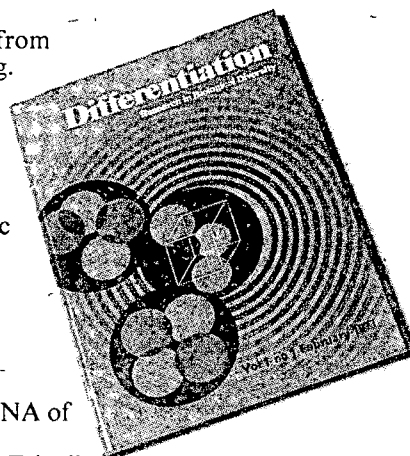
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(1461)

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FIELD: RESIDENTIAL ENVIRONMENT

GENERAL. The Division has a total staff in excess of 300 including some 150 professional scientists. It undertakes research for the benefit of the Australian community into the theory, techniques and economics of building and community design, construction and materials development and is seeking an understanding of the interaction between the built environment and people. Programmes for studying the built environment are being developed in the context of both urban communities and remote settlements. The appointee will be located at Highett, Victoria.

DUTIES. To conduct research into the effects of the built environment, the relevant aspects of the natural environment and related factors of community living on residents of urban and remote settlements in Australia. This will involve the development of research techniques capable of providing guidance to physical and social planners and others determining the nature of human settlements.

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DIVISION OF CLOUD PHYSICS

FIELD: ATMOSPHERIC PHYSICS

GENERAL. Current investigations in the Division (located in Sydney, N.S.W.) are concerned with the distribution and properties of atmospheric nuclei, basic and experimental studies of the physical processes which lead to cloud and rain and evaluation of the feasibility of modifying precipitation by cloud seeding.

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Reference Number 425/10

DUTIES. To investigate the size, distribution, chemical nature and sources of those particles on which cloud drops

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QUALIFICATIONS. A Ph.D. degree, or equivalent qualifications, in physics, or an allied experimental field, together with demonstrable research ability. Experience in atmospheric physics, meteorology or aerosol technology would be an advantage.

Reference Number 425/11

DUTIES. To determine concentrations, size distribution and nature of all particles in the stratosphere or at clean sites in the lower atmosphere in order to provide a reference level for the assessment of changes induced by such factors as increased air traffic or industrialization. The appointee will be required to visit inland sites from which sampling balloons are released. Work on the development and calibration of suitable samples will be necessary.

QUALIFICATIONS. A Ph.D. degree, or equivalent qualifications, in physics, or an allied experimental field, together with demonstrable research ability. Experience in atmospheric physics, meteorology or aerosol technology would be an advantage.

DIVISION OF APPLIED CHEMISTRY

Reference Number 586/168

FIELD: MICROBIOLOGY/BIOCHEMISTRY ENGINEERING

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TOXICOLOGY UNIT

Toxicologists

Graduates with a special interest in the pharmacological aspects of toxicology and drug safety evaluation. Relevant qualification would be a Pharmacology Degree or M.I. Biol. backed up by experience in physiology or pharmacology—not necessarily related to toxicology or drug safety assessment. Preferred age range 24–30.

Two graduates are also required in the Animal Studies Section. Relevant degrees could be physiology, biochemistry, pharmacology or M.I. Biol. Experience in drug safety and toxicology procedures an advantage but those appointed could be new graduates in the age range 21–30.

Pathologist

With experience in the evaluation of histo-pathology from laboratory animals treated with new drugs. The successful candidate could hold a veterinary qualification or be a physiologist with training in slide reading.

Mutageneticist

A graduate in a biological discipline with a specialist interest in genetics. Some experience of testing new drugs for mutagenic potential an advantage but encouragement and specialist training will be given to increase expertise where necessary.

Research Assistants

1. Animal Studies

Minimum qualification HNC/L.I. Biol. Some experience in drug safety and toxicology procedures in a pharmaceutical

or university laboratory essential, including handling laboratory animals. Age 23–35.

2. Clinical Chemistry

Minimum qualification HNC Experience of clinical chemistry laboratory techniques essential, possibly gained in pharmaceutical laboratories studying drug safety and toxicology or in a hospital laboratory pathology department. Age 20–30.

BASIC RESEARCH-PROJECT TEAMS

Pharmacologists

To join multi-disciplinary teams of scientists and technicians seeking novel therapeutic compounds in the anti-hypertension, anti-inflammatory and gastric secretion areas.

Synthetic Organic Chemists

To work in a project group investigating compounds of potential pharmaceutical interest. Applicants must have a good honours degree, preferably with one or two years experience in the field of synthetic organic chemistry—biased, towards medicinal research. We would also be interested to hear from those currently completing Ph.D. theses.

Biochemical Pharmacologist

With a degree level training in Biochemistry and a good grounding in general pharmacology.

Competitive salaries will be paid and there are the usual benefits which are associated with a major British-based company. The Medicinal Research Centre is located one mile from Harlow New Town and combines easy access to London with proximity to pleasant countryside. Development Corporation housing may be available at economic rent to suitable candidates.

Please write, outlining your career to date, to:
John Atkinson, Personnel Officer,
Beecham Research Laboratories, Fourth Avenue,
The Pinnacles, Harlow, Essex.



1872
(1517)

BRL

CHELSEA COLLEGE UNIVERSITY OF LONDON

DEPARTMENT OF APPLIED BIOLOGY

TECHNICIAN (GRADE 3) required in the Microbiology Laboratory. Duties will include assistance in the preparation of media, reagents and cultures for undergraduate teaching, assistance in the research activities of the Microbiology Section, and the technical photography of the Department. Previous experience in microbiology (preferably bacteriology) is required. Salary scale £1,825 to £2,095 per annum (including London allowance). Application forms from Mr. K. Harris (N), Department of Applied Biology, Hortensia Road, London SW10 0QX. (1486)

RESEARCH TECHNICIAN REQUIRED IN THE Department of Plant Biology and Microbiology to assist in higher plant genetics and cytogenetics. Salary (Grade 3) £1,650 by £54 to £1,794 per annum, plus London Weighting £175 per annum. Five-day week. Five weeks (in total) annual leave—(T/JSF). Queen Mary College, Mile End Road, London E1 4NS, stating age, experience, qualifications and present work. (1487)

WINDSOR GROUP H.M.C. AREA LABORATORY KING EDWARD VII HOSPITAL WINDSOR

Applications are invited for the following posts:

(a) **DEPARTMENT OF MICROBIOLOGY:** 1. Senior Technician. 2. Technician. 3. Junior Technicians—for this and the two undermentioned departments.
(b) **DEPARTMENT OF HAEMATOLOGY:** Technician.

(c) **DEPARTMENT OF CHEMICAL PATHOLOGY:** Technician.
Good facilities for those wishing to take special Finals.

The Laboratory provides a comprehensive service for approximately 1,000 beds in the Windsor, Ascot and Maidenhead areas, and for Outpatient Clinics and General Practitioners in the area. Expansion of the Hospital Services is anticipated in the near future. The hospital is situated close to public terminal, within easy access of London by road and has its own swimming pool. Applications to the Senior Pathologist, Area Laboratory. Tel. Windsor 61424 (enquiries to Senior Chief Technician). (1508)

PHYSIOLOGIST UNIVERSITY OF TORONTO CANADA

DEPARTMENT OF OPHTHALMOLOGY RESEARCH INSTITUTE

offers a lectureship in ocular physiology. Salary \$10,000 for 12 months, renewable.
Apply: Professor J. C. McCulloch, Department of Ophthalmology, 1 Spadina Crescent, Toronto, Ontario, Canada M5S 2I5. (1472)

CHARING CROSS HOSPITAL MEDICAL SCHOOL

GRADUATE/TECHNICIAN required for a varied research programme in the Department of Obstetrics and Gynaecology, involving Haematology, and some Biochemistry and Histochemistry. Previous experience not essential. Salary £1,500 per annum, post tenable for one year in the first instance with probable extension for a suitable individual. Please apply with curriculum vitae to: The Secretary, Charing Cross Hospital Medical School, Brandenburg House, Fulham Palace Road, W6 9HH. (1474)

UNIVERSITY OF MELBOURNE
LECTURESHIPS (LIMITED TENURE)
(3) IN MARINE SCIENCE

The University, in recognizing the importance of the Marine Sciences in teaching and research, invites applications for lectureships tenable for three years in each of the fields of Marine Botany, Marine Chemistry and Marine Zoology and commencing January 1, 1974. Applicants should hold a Ph.D. or its equivalent.

The appointments will be made to the Faculty of Science and the appointees will work within appropriate Departments in the Faculty of Science and should have interests which might assist with the further development of Marine Science in the University of Melbourne. In particular they will be expected to become involved in the planning of new courses, maintain a personal research programme, and supervise research.

LECTURESHIP IN MARINE BOTANY

QUALIFICATIONS: To include postgraduate degree in Botany and research experience in Marine Botany (Phytoplankton or an allied field) and an interest in both teaching and research.

DUTIES: Primarily to initiate an undergraduate course and research in phytoplankton to be integrated with existing course in Marine Botany and with other aspects of Marine Science taught in the Science Faculty. It is expected that the appointee will engage in research and be available for limited teaching in other areas such as First Year Biology.

LECTURESHIP IN MARINE CHEMISTRY

QUALIFICATIONS: Applications are invited from candidates who have majored in Chemistry or Marine Chemistry, and who preferably have had post-doctoral research experience in one of the areas of analytical, biological, electrolyte or membrane chemistry. Preference may be given to a candidate whose research interests complement existing Departmental programmes.

DUTIES: The appointee will be expected to lecture in Marine Chemistry and supervise a practical unit in marine chemistry to undergraduate students. About half the appointee's time will be available for collaborative research in programmes in Marine Chemistry.

LECTURESHIP IN MARINE ZOOLOGY

QUALIFICATIONS: Ph.D., or equivalent, in an area of Marine Zoology, preferably Ecology, or a serious intention to specialize in that subject; experience in teaching at an advanced undergraduate level desirable; and recognized research achievement.

DUTIES: Establishment of a third-year level unit in Marine Zoology; co-ordination and participation in a general inter-disciplinary unit in Marine Ecology; and limited teaching in other areas of Zoology.

SALARY: \$A8,698 to \$11,982 per annum.

Details of application procedure and conditions of appointment may be obtained from the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close on December 10, 1973.

(1514)

UNIVERSITY OF MELBOURNE
LECTURESHIP IN THE DEPARTMENT
OF PHYSIOLOGY

Applications are invited for this position.

QUALIFICATIONS: The applicant should have teaching and research experience in Physiology and a Ph.D. in Physiology, a Medical Degree or equivalent.

DUTIES: The appointee will participate in the departmental teaching activities, including the organizing and supervision of laboratory exercises for undergraduate students. It is anticipated that the appointee's research interests relate to one of the fields being studied at present in the Department. These include: physiology of the mammalian nervous system with emphasis on sensory processes, lipid metabolism and atherosclerosis, cardiovascular, respiratory and renal physiology, haematology and biomedical instrumentation.

SALARY: \$A8,698 to \$11,982 per annum.

COMMENCING DATE: March 1, 1974, or as soon as possible thereafter.

Further details may be obtained from Professor I. Darian-Smith, Department of Physiology, in the University.

Application procedure together with conditions of appointment may be obtained from the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close on December 14, 1973.

(1511)

THE ROYAL VETERINARY COLLEGE
(UNIVERSITY OF LONDON)

TECHNICIAN (Grade 6) in Biochemistry required to supervise teaching and research laboratories in the Department of Physiology. Technical and administrative skills are of equal importance in this post.

Salary on scale £2,370 by £84 to £2,874 per annum.

Application to Assistant Secretary (Personnel) (N), The Royal Veterinary College, Royal College Street, London NW1 0TU.

(1513)

Opportunities Overseas

This appointment is wholly financed by the British Government under Britain's programme of aid to the developing countries.

Ghana

WEED CONTROL SPECIALIST

To initiate and implement a research programme covering forest and savanna zones. The programme will involve a detailed study of advanced weed control methods, particularly the use of herbicides in conjunction with optimal agronomic practices in the cultivation of field and plantation crops. Applicants who should normally be citizens of, and permanently resident in, the UK should have a degree with preferably postgraduate training and extensive experience in weed research. Knowledge of tropical agronomy and weed problems desirable. Appointment two tours of 18 months.

Salary, subject to UK income tax, in range of £3,000-£4,500 pa plus a variable tax free overseas allowance in range of £725-1,480 pa.

Other benefits include free family passages, paid leave, children's education allowances and free accommodation and medical attention.

For full details, application form and booklet about Ghana, please apply giving age and brief details of qualifications and experience to:—

Appointments Officer,
Foreign and Commonwealth Office,

Overseas Development Administration

Room E301/N, Eland House,
Stag Place, London SW1E 5DH

(1509)



ARCHIFAR

A Pharmaceutical Industry

has a vacancy at the new Research Laboratories in Northern Italy for a

MICROBIOLOGIST

He will be engaged in research on ANTIBIOTICS and ENZYMES. Applicants must have at least 4 years of post-graduate experience in the field. Applications which should include comprehensive curriculum vitae and addresses of two referees, should be sent to:

Archifar S.p.A., Via Trivulzio, 18, 20146 Milan, Italy.

(1387)

UNIVERSITY OF LEICESTER DEPARTMENT OF PHYSIOLOGY

SENIOR LECTURER

Applications are invited for the post of SENIOR LECTURER in the Department of Physiology (Head of Department, Professor R. Whittam, F.R.S.). Experience and an interest in teaching medical students are essential. Preference will be given to holders of a medical qualification, but other suitably qualified applicants will be seriously considered. There are excellent research facilities.

Initial salary, dependent on qualifications and experience, within the scale £4,368 to £5,496 a year, with F.S.S.U. membership.

Further particulars from the Registrar, to whom applications should be sent by December 11.

(1423)

Assistant in Regulatory Affairs Department

Smith Kline & French Laboratories Limited is a major international pharmaceutical company based in Welwyn Garden City. We now require an additional graduate to join our Regulatory Affairs Department, which is the principal interface between the company and the medicines licensing authorities.

The basic requirements are:

a good honours degree in a biological science or pharmacy with, possibly, postgraduate experience in pharmacology

the ability to present information in coherent, precise reports.

The work will entail the evaluation and editing of data from within the Company's own research and from other sources. Experience in the preparation of data for licensing bodies or experience with the requirements of the drug regulatory authorities would be a distinct advantage.

Salaries are competitive and will reflect ability and experience. Conditions of employment are in line with those expected of a large international organisation. Assistance with relocation expenses given where appropriate.

Please write giving brief relevant details to:

**The Personnel Officer,
Smith Kline & French Laboratories Limited,
Mundells, Welwyn Garden City, Herts.**

(1476)



BIOLOGICAL SCIENCES Quality Control Manager

for Flow Laboratories, Europe's leading supplier of tissue cultures, media, sera and viral diagnostic reagents. The company manufactures in sterile conditions and quality considerations are paramount. The Quality Control Manager will be responsible to the Scientific Director for implementing — and where necessary modifying — quality control procedures covering raw materials, production processes and finished goods. Candidates, probably aged 25 to 30, will be life science graduates, preferably qualified to Ph.D. level, having specialised in a relevant aspect of virology, microbiology, bacteriology or biology. Previous experience of operating quality control techniques would be an asset. Salary by agreement; excellent pension and assistance with removal to West of Scotland. Please write in strict confidence with brief career details to A.W.B. Thomson, 12 Lynedoch Crescent, Glasgow G3 6EQ.

SELECTION ● THOMSON

(1462)

Department of the Environment
Water Pollution Research Laboratory, Stevenage

Information Scientist

■ Edit and prepare technical reports ■ Prepare material for exhibitions ■ Literature searching and information retrieval ■ Answer technical enquiries.

□ Degree, HNC or equivalent in Biology, Physics, Chemistry or related subject □ Age under 27 □ Appointment as Scientific Officer (£1318-£2177) □ Ref: SA/9/HE □ Closing date 30 November 1973.
□ Application forms from Establishments Office, Water Pollution Research Laboratory, Elder Way, Stevenage, Herts.

Centre for Overseas Pest Research, London

Statistician/Biometrician

■ To work in Ecology Division ■ Advise research workers on collection and presentation of experimental data on insect and bird pests ■ Involves working abroad for at least short periods.

□ Degree, preferably in Mathematics, with training in Statistics and interest in Biology □ Interest in computer programming and building of insect population models desirable □ Age under 32 □ Appointment as Scientific Officer (£1493-£2352); Higher Scientific Officer (£2251-£2842); or Senior Scientific Officer (£2790-£3815) □ Ref: SA/5/JA □ Closing date 30 November 1973.

□ Application forms from the Establishment Officer, Centre for Overseas Pest Research, Overseas Development Administration, College House, Wrights Lane, London W8 5SJ.

Department of the Environment
Princes Risborough Laboratory

Technical Editor

■ Assist in editing publications ■ Prepare drafts for articles and press releases on the Laboratory's work (timber and related technology) ■ Arrange dissemination of research results through scientific and technical journals.

□ Degree/HNC in science or engineering □ Editing and technical writing experience and knowledge of timber technology advantageous □ Age under 27 □ Appointment as Scientific Officer (£1318-£2177) □ Ref: SA/34/HA □ Closing date 30 November 1973.

□ Application forms from Establishment Office, Princes Risborough Laboratory, Princes Risborough, Aylesbury, Bucks.

Science
group
CIVIL SERVICE

(1504)

UNIVERSITY OF YORK
DEPARTMENT OF BIOLOGY

Applications are invited for the post of TECHNICAL in the Biology Department teaching laboratories. Candidates will be responsible to the Chief Technician in the teaching laboratories and should have an Advanced City and Guilds Certificate, H.N.C. or equivalent qualification.

Salary in Grade 4 (£1,848-£2,163).

Applications to Departmental Superintendent, Biology Department, University of York, Heslington, York YO1 5DD, with the names and addresses of two referees by November 16. (1522)

UNIVERSITY OF TORONTO
DEPARTMENT OF PHYSICS

Applications are invited for a faculty position at the level of ASSISTANT PROFESSOR in the Department of Physics. Applicants should have a Ph.D. and research experience in solid earth physics. The solid earth physics group in the Department of Physics has an active and well supported research programme in geomagnetism, crustal seismology, tectonics and geochronology, and works in close co-operation with the Department of Geology. Appointment will be effective July 1, 1974.

Applicants should send curriculum vitae and names of three referees to: Professor D. J. Rowe, Department of Physics, University of Toronto, Toronto M5S 1A7, Ontario, Canada. (1439)

UNIVERSITY OF BATH
SCHOOL OF BIOLOGICAL SCIENCES

Applications are invited for a

RESEARCH ASSISTANT

to assist in an investigation, supported by the Science Research Council, into the Physiology of Lampreys. Candidates should have some experience of basic biochemical techniques and have a degree or HNC qualification. Salary range: £1,650 to £1,920. Application forms obtainable from the Registrar (S), The University, Bath BA2 7AY, quoting reference number 73/149. Closing date: December 10, 1973. (1465)

INSTITUTE OF OPHTHALMOLOGY
(UNIVERSITY OF LONDON)
EDITORIAL ASSISTANT

Editorial Assistant required by Editor of international medical abstracting journal to assist in the production of the journal. Applicants should be educated to "A" level standard. A knowledge of modern languages and an ability to type would be an advantage. Previous editorial experience not essential. Age 20 plus. Starting salary £1,554 per annum. 5-day week, 9.00 a.m. to 5.30 p.m. Four weeks annual leave.

Applications in writing should be made to: The Secretary, Institute of Ophthalmology, Judd Street, London WC1H 9QS. (1477)

BIOLOGIST

Applications are invited for a full-time opening in the Cell Biology Division for a well-trained Ph.D. interested in committing his/her efforts to developing organ culture systems to investigate the differentiation and altered differentiation of epithelial tissues in response to vitamin A, vitamin A analogues, and carcinogens.

Should have training and background in organ/tissue culture, a good basic biological training, and be acceptably knowledgeable in biochemistry. A recent Ph.D. or one with one to two years' post-doctoral training would be acceptable.

Please send recent curriculum vitae to:

Personnel Office
Southern Research Institute
2000 Ninth Avenue South,
Birmingham, Alabama 35205, U.S.A.

An Equal Opportunity Employer M/F.

(1389)

THE UNIVERSITY OF MELBOURNE

LECTURER/SENIOR LECTURER IN VETERINARY ANATOMY

in the

Department of Veterinary Preclinical
Sciences

Applications are invited for this position from graduates who have specialised in the study of morphology and are interested in teaching veterinary undergraduates in the field of gross anatomy. The appointee will be expected to assist with lecturing and practical instruction in anatomy and to engage in research in projects with anatomical implications within the departmental framework which includes physiology, biochemistry, pharmacology and developmental and microscopic anatomy.

Salary: Lecturer, \$A8,698 to \$A11,982; Senior Lecturer, \$A12,268 to \$A14,308.

Further information, including details of application procedure and conditions of appointment, is available from the Registrar, The University of Melbourne, Parkville, 3052, Victoria, Australia. Applications, referring to position 260008, should be addressed to the Registrar, and close on December 14, 1973. (1475)

UNIVERSITY OF EXETER
DEPARTMENT OF ENGINEERING SCIENCE
RESEARCH IN BIO-ENGINEERING

A research studentship is available in the Department of Engineering Science, University of Exeter. The value of the studentship is £1,063 per annum and is available for a period of three years in the first instance.

The work will be concerned with an examination of the properties of bone, bone cement and implants under various loading conditions to determine the optimum properties of bone cements and the optimum method of transmitting loads through an implant into bone.

Applications are invited from science and engineering graduates with first or upper second class honours degrees.

The applications, giving details of the candidate's qualifications and experience, and the names of two referees, should be addressed to: The Secretary of the University, The University of Exeter, Northcote House, The Queen's Drive, Exeter EX4 4QJ. (1467)

ENTERIC REFERENCE LABORATORY

Honours Science Graduate, at least 2:1, in a biological subject or a basic science; if latter, knowledge of molecular biology necessary. Work is in a research group investigating problems connected with transferable drug resistance. Post-doctoral applicants eligible. Starting salary dependent on qualifications and experience from minimum of £1,566 plus £126 London Weighting per annum (plus wage award being negotiated).

Applications with full curriculum vitae and names and addresses of at least two referees to Personnel Officer, Central Public Health Laboratory, Colindale Avenue, London NW9 5HT. (1500)

INSTITUTE FOR MARINE ENVIRONMENTAL RESEARCH

The research programmes of I.M.E.R. are centred on ecological surveys of the open ocean, near-shore waters and estuaries, including field and laboratory studies of the factors which generate variability in ecosystems.

Applications are invited for three posts:

K—COASTAL OCEANOGRAPHER to join a group of biologists and chemists engaged in a systems study of estuarine ecology, presently in the Bristol Channel: to take responsibility for studies of circulation patterns and water budgets, including long-term, climate-induced variability. To be based at Plymouth.

QUALIFICATIONS: Degree in a physical science, preferably with relevant experience, ability in computer handling of data and a general understanding of, and sympathy with, simulation modelling techniques.

L—OCEANOGRAPHER to join a group of biologists and physicists investigating long-term trends in the plankton populations of the North Atlantic: to specialize in analysis of long-term climatic changes in the oceanic environment and in the correlation of such changes with trends in plankton populations observed from the I.M.E.R. Continuous Plankton Recorder Surveys. To be based at Edinburgh.

QUALIFICATIONS: Degree in a physical science, preferably with training or experience in physical oceanography or climatology and computerized data handling techniques.

M—ECOLOGIST for research on long-term trends in the plankton of the North Atlantic based on the Continuous Plankton Recorder Survey: to specialize in studies of variability of plankton community structure related to environmental variability. To be based at Edinburgh.

QUALIFICATIONS: Degree in a relevant biological science, and preferably with training in computer handling and analysis of data.

Grades and starting pay dependent on age, qualifications and experience. Candidates will be considered for appointment at Higher Scientific Officer/Senior Scientific Officer level (salary range £2,076 to £3,640) and exceptionally well qualified candidates will be considered for Principal Scientific Officer (£3,472 to £4,575).

Non-contributory pension scheme.

For application forms or further particulars write (specifying post K, L or M) to the Director, Institute for Marine Environmental Research, 13/14 St. James Terrace, Plymouth PL1 3AX, Devon.

Closing date: November 30, 1973.

NATURAL ENVIRONMENT RESEARCH COUNCIL. (1503)

UNIVERSITY OF SYDNEY LECTURESHIPS IN PHYSIOLOGY (TWO)

One person appointed will be required to assist in the teaching of physiology to medical, dental and science students and to take special responsibility for the development of teaching methodology including the use of audio-visual aids, programmed texts and assessment techniques.

The other will be required to assist in the teaching of medical, dental and science students and will also be required to take responsibility for the recently acquired Philips 201 electron microscope and to advise and assist other members of the department in its use.

The positions advertised are permanent, but may be filled for three years in the first instance with possibility of permanency or in certain cases return fares.

Salary range: \$A8,698 to \$A11,982 per annum.

Applications including curriculum vitae, list of publications and names of three referees by November 20, 1973, to the Registrar, University of Sydney, N.S.W. 2006, Australia, from whom further information available. Information about conditions of appointment and application procedure also available from Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF. (1483)

STRANGEWAYS RESEARCH LABORATORY WORT'S CAUSEWAY CAMBRIDGE CB1 4RN

Applications are invited for the post of RESEARCH ASSISTANT in the Tissue Physiology Department.

The work will be concerned with a study of the role of extracellular proteolytic enzymes in invasive human tumour growth. Applicants should have an honours degree in the biological sciences, preferably with an interest in immunology and/or biochemistry. The work will involve the use of immunological and immuno-cytochemical methods and cell and organ culture techniques.

The successful applicant will be expected to start in January 1974. The salary starts at £1,830 per annum (plus F.S.S.U.) and rises to £2,058 over 3 years.

Applications, outlining previous experience and including the names of two referees, should be sent to Dr. A. R. Poole at the above address. (1493)

NATURE

Secretary to the Editor

This is a senior secretarial position with administrative responsibilities. It would be of most interest to someone with a scientific background.

Write to the Editor, NATURE,
4 Little Essex Street, London WC2R 3LF

A SCIENTIFIC OFFICER

is required to undertake the design and layout of investigations conducted at the Board's Experimental Station, prepare working documents and subsequently process, analyse and report the data. He or she will also assist in the interpretation of the results obtained from research sponsored by the Board at other research centres and universities.

Applicants should preferably have a degree in Agriculture, Agricultural Science or related biological discipline, with experience in field experimentation and analysis of data. Knowledge of data processing techniques would be advantageous. Salary will be within the scale £2,112 to £2,745 per annum, dependent upon age, qualifications and experience, plus London allowance of £177 per annum. Pension scheme. Luncheon vouchers.

Application form from Personnel Officer, Potato Marketing Board, 50 Hans Crescent, Knightsbridge, London SW1X 0NB. (1495)

THE INSTITUTE OF PHYSICS requires an EDITORIAL ASSISTANT to join its permanent staff in Bristol

The Publishing Division of the Institute has a staff of about 60, many of whom are professionally qualified. The main activity is the publication of a range of international physics journals, and there are plans for expansion in this and related areas.

Applicants should be prepared to work steadily as a member of a small editorial team. Working conditions are pleasant, in a modern office.

Candidates should have an honours degree or equivalent in physics, mathematics or chemistry. Starting salary will be between £1,440 per annum (minimum for a recent graduate) and £1,800 per annum with regular increases to £2,340 per annum and promotion prospects to £2,940 per annum. No previous editorial experience is required. Training will be given in the basic techniques of sub-editing and proof reading, with the possibility of further training in wider aspects of publishing.

Apply to: Managing Editor, Institute of Physics,
Netherton House, 23 Marsh Street,
Bristol BS1 4BT. (1518)

CHAIRMAN—DEPARTMENT OF ANATOMY

Columbia University, College of Physicians and Surgeons, an equal opportunity employer, is seeking an individual as Chairman of Anatomy Department. Should be qualified medical scientist and experienced medical educator.

Send curriculum vitae to: Myron Wlnick, M.D., Chairman, Search Committee, Institute of Human Nutrition, 511 West 166th Street, New York, New York 10032. (1289)

JUNIOR TECHNICAL OFFICER REQUIRED AT Pollards Wood Research Station of the Institute of Cancer Research, Chalfont St. Giles, Bucks., to take part in a research programme on mutagenic effects of carcinogens. B.Sc. or H.N.C. in a biological subject. Experience in genetics, cytology or cell biology desirable. Further study possible. Starting salary £1,400 per annum in a scale extending to £2,073, according to qualifications, age and experience.—Apply in duplicate, giving the names of two referees, to the Secretary, 34 Summer Place, SW7 3NU, quoting Ref. 301/B/490. (1489)

PLANT PATHOLOGIST

Applications are invited for the permanent post of Plant Pathologist in the Plant Pathology Division of the Ministry of Agriculture, to conduct research on fungal diseases of potatoes.

The person appointed may be required to undertake teaching duties in the Department of Mycology and Plant Pathology, Faculty of Agriculture and Food Science, Queen's University, Belfast.

Appointment may be at Senior Scientific Officer, Higher Scientific Officer or Scientific Officer level.

The necessary qualifications are:

Senior Scientific Officer—normally over 25 and under 32 years of age with a good Honours Degree in a scientific or agricultural discipline pertinent to plant pathology with at least 4 years relevant postgraduate experience. Salary scale £2,615–£3,640.

Higher Scientific Officer—under 30 years of age with a good Honours Degree as above and at least 2 years relevant postgraduate experience. Salary scale £2,076–£2,667.

Scientific Officer—under 27 years of age with a good Honours Degree as above. Salary scale £1,318–£2,177.

Grading and entry point to salary scales will be related to qualifications and experience.

Please write or telephone for an application form and further information quoting Ref. SB 234/73/N to: Civil Service Commission, Clarendon House, Adelaide Street, Belfast BT2 8ND (telephone 0232-44300, ext. 26). Completed applications must be returned to arrive not later than 27th November, 1973.



**NORTHERN IRELAND
CIVIL SERVICE**

(1497)

Plant Physiologist— Liberia

Circa £6,200

The Firestone Plantations Company who operate in Liberia the largest single plantation in the world require a plant physiologist to assist in the continuous development programme of improving the quality and yield of the product. Candidates should have a good degree in botany, forestry or agriculture and good knowledge of hevea culture, tapping systems and plant stimulation. Salary and local allowances are payable in U.S. dollars and will not be less than £6,200 per annum. Home leave each year, subsidised housing, free medical and educational facilities are among the many fringe benefits provided. Interviews are being arranged for mid-November and applicants should write in confidence to:

**Staff Personnel Manager,
Firestone Tyre & Rubber Co. Ltd.,
Great West Road,
Brentford, Middx.**



(1482)

**CENTRAL PUBLIC HEALTH
LABORATORY
COLINDALE AVENUE, LONDON NW9 5HT**

Honours Science Graduate, microbiology, for position of **QUALITY CONTROLLER** in Media Production Department. The successful applicant will be responsible for routine testing and control of bacteriological and virological media; also the development of new media. Experience in microbiology with particular reference to medical bacteriology advantageous. Participation in some administration duties is expected. Salary according to age, qualifications and experience. Applications with full curriculum vitae to Personnel Officer at above address.

(1499)

UNIVERSITY OF KHARTOUM SUDAN

Applications are invited for the post of **PROFESSOR/SENIOR LECTURER** in the **DEPARTMENT OF ANIMAL PRODUCTION**, Faculty of Agriculture. The applicant should be a holder of an M.Sc. or Ph.D. in the field of Animal Nutrition and Feeding and have a good experience with feed-lot fattening and meat quality assessment. He will be offered the post of a Senior Lecturer or Professor depending on his qualifications, publications and experience. Salary scale: Professor £53,600 per annum; Senior Lecturer £52,400 to £52,800 per annum. The British Government may supplement salary in range £1,300 to £1,800 per annum (sterling) for married appointee or £800 to £1,000 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. Family passages; various allowances; superannuation scheme; annual overseas leave. Detailed applications (2 copies) including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than November 29, 1973, to the Personnel Secretary, University of Khartoum, P.O. Box 321, Khartoum, Sudan. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars are available from either address.

(1488)

UNIVERSITY OF OTAGO DUNEDIN, NEW ZEALAND ASSISTANT LECTURER IN MICROBIOLOGY

The Council of the University of Otago, Dunedin, New Zealand, invites applications from science graduates for an appointment as Assistant Lecturer in the Department of Microbiology in the Medical School. This appointment is for up to three years. Salary: according to qualifications and experience—\$NZ4,660 to \$5,839 per annum.

Further information may be obtained from the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF, from Professor J. A. R. Miles, Department of Microbiology, University of Otago Medical School, P.O. Box 913, Dunedin, New Zealand, or from the Registrar of the University, P.O. Box 56, Dunedin, New Zealand.

Applications close in New Zealand and in London on December 1, 1973.

(1512)

McMASTER UNIVERSITY VIROLOGIST

A position is available for a Virologist at the Assistant or Associate Professor level. The appointee will be part of a viral oncology group being formed at McMaster University as well as a member of the Department of Biology. His/her research interests should be the molecular biology and/or genetics of animal viruses. His/her primary responsibility will be research and supervision of graduate students.

Applicants should send their curricula vitae and the names of three referees to the Chairman, Department of Biology, McMaster University, Hamilton, Ontario L8S 4K1, Canada, to arrive no later than January 15, 1974.

(1381)

UNIVERSITY OF MANCHESTER DEPARTMENT OF ZOOLOGY RESEARCH ASSISTANT IN CYTOLOGY

Applications invited for this post (funded by the O.D.A.) for research connected with tsetse fly and trypanosome control, involving the investigation of DNA/RNA synthesis during gametogenesis, oogenesis and vitellogenesis, and the cytogenetics of species, hybrids and radiation induced mutants. Post tenable until September 30, 1976, with an initial salary up to £2,058 per annum rising to £2,388 per annum. F.S.S.U.

Detailed applications, with names of two referees, should be sent to Dr. D. I. Southern, Department of Zoology, The University, Manchester M13 9PL, as soon as possible.

(1404)

**ST. THOMAS'S HOSPITAL
MEDICAL SCHOOL
(UNIVERSITY OF LONDON)
LONDON SE1 7EH**

Applications are invited from suitably qualified graduates for appointment as ASSISTANT LECTURER in Medical Genetics. This newly established post will be held within the Department of Anatomy. The successful candidate will be expected to take part in teaching medical genetics, to assist in building up a cytogenetics unit giving a service to the hospital and to pursue a research interest. Appointment is for three years in the first instance with a possible extension to four years; salary, according to age, qualifications and experience, but within the range £1,929 to £2,223 per annum plus £162 per annum London allowance and superannuation with F.S.S.U. Some postgraduate experience, with or without a Ph.D. is desirable but not essential. Applications giving full details to be sent to School Secretary. (1494)

**AGRICULTURAL RESEARCH COUNCIL
INSTITUTE FOR RESEARCH ON
ANIMAL DISEASES
COMPTON, BERKSHIRE
HELMINTHOLOGIST**

Applications are invited from graduates with at least an upper second class honours degree and a minimum of two years' research experience for a vacant post in the Institute's Department of Parasitology. Preference may be given to a candidate who has obtained a Ph.D. degree. The successful candidate will be required to conduct research on nematodes of farm livestock and initially will be expected to study nematode/bacterial interactions. The appointment will be in the H.S.O. (£2,076 to £2,667)-S.S.O. (£2,615 to £3,640) scales according to qualifications and experience, plus a 4% per cent allowance to offset F.S.S.U. superannuation contributions. Applications, accompanied by a curriculum vitae and the names and addresses of two referees, should be submitted to the Institute Secretary, citing vacancy No. 153, by November 30, 1973. (1496)

**UNIVERSITY OF OTAGO
DUNEDIN, NEW ZEALAND
LECTURER OR SENIOR LECTURER
IN NUTRITION**

Applications are invited for the position of Lecturer or Senior Lecturer in the Department of Nutrition in the School of Home Science, University of Otago.

Salary: Lecturer: \$NZ6,575 to \$8,343 per annum; Senior Lecturer: \$NZ8,489 to \$NZ10,846 per annum with a bar at \$NZ9,963 per annum. (Note: \$NZ100 equals approximately £61 sterling; \$US147; SA100.)

Applicants should be graduates in Science with specialisation in biochemistry, physiology, nutrition or chemistry; Food Sciences or in Home Science.

Further particulars are available from the Secretary-General, Association of Commonwealth Universities (Apps.), 36 Gordon Square, London WC1H 0PF, or from the Registrar of the University.

Applications close in New Zealand and London on February 15, 1974. (1510)

**UNIVERSITY OF OXFORD
TRINITY COLLEGE
JUNIOR RESEARCH FELLOWSHIP
IN BIOLOGICAL OR MEDICAL
SCIENCE**

The College invites applications for a Junior Research Fellowship in a field of science related to biology or medicine, tenable for three years from October 1974. The Fellowship is intended for work of post-doctoral character; preference will be given to candidates under 30 years of age. Further details are available from the College Secretary. The closing date for applications is January 5, 1974. (1516)

**MEDICAL RESEARCH COUNCIL NATIONAL
Institute for Medical Research. BIOCHEMIST.** Applications are invited for a postdoctoral appointment on the staff of the DIVISION OF MOLECULAR PHARMACOLOGY to work on enzymological and structural aspects of membrane bound receptors. The appointment will be for three years in the first instance. Incremental salary according to age and qualifications within the range £2,058 to £4,548 per annum plus £162 per annum London allowance. F.S.S.U. provision. Applications, giving the names of two professional referees, should be sent to the Director, National Institute for Medical Research, Mill Hill, London NW7 1AA. (1519)

MALE GRADUATE (OR H.N.C.) BIOLOGIST required to join a team working in respiratory physiology and inhalation toxicology. Studies are being made into the effects on Primates and Rodents of exposure to cigarette smoke, air pollutants, and therapeutic aerosols. Salary range £1,400-£2,800 depending upon experience.—Application form from: John Halliday, Personnel Officer, Huntingdon Research Centre, Huntingdon PE18 6ES, quoting Reference 279. (1448)



Pharmaceuticals Division

Technical Assistant

We are looking for someone with experience of the microbial field (virology and/or bacteriology) to work in our Virus Section of Biology Department. The main responsibility of the job is to develop potential antiviral drugs. In addition, the job involves some diagnostic work in connection with animal health, and also fundamental research into the control of human and animal virus disease.

The job would suit someone with a technical background (IMLT), but paper qualifications are less important than a lively mind and a willing and constructive approach to the problems of the job.

The Pharmaceuticals Division is very attractively situated in rural North Cheshire, within easy reach of main road and rail routes. There is a wide range of country and town housing within 20 minutes drive to cater for most tastes. Conditions of service, career opportunities, and assistance given to married men in moving home are designed to attract and retain staff of high calibre.

Applications in writing, giving brief details of age, qualifications and experience, should be addressed to:

**M F Losse Personnel Officer
Imperial Chemical Industries Limited
Pharmaceuticals Division
Merseydale Park
MACCLESFIELD Cheshire SK10 4TG.**

(1505)



1946 1967 1968 1969 1970 1972

**COLÁISTE NA HOLLSCOILE GAILLIMH
(University College Galway)**

TECHNICIAN

The Department of Obstetrics and Gynaecology has a vacancy for a Technician.

Salary within the region of £1,614 by £54 to £1,830.

Minimum qualifications: Intermediate Certificate of Institute of Medical Laboratory Technology, Intermediate Certificate of City and Guilds of London, Intermediate Technological Certificate of Department of Education or equivalent.

Applications, stating age, experience, qualifications and the names of two referees, should be sent, as soon as possible, to Professor of Obstetrics and Gynaecology, Regional Hospital, Galway.

(1459)

**UNIVERSITY OF NATAL
DEPARTMENT OF GEOLOGY, DURBAN**

Applications are invited from suitably qualified persons for appointment to the post of:

LECTURER IN ECONOMIC GEOLOGY

The salary scale attached to the post is:

R4,800 by R300 to R6,900 per annum

plus 15 per cent pensionable allowance on basic salary.

The commencing salary notch will be dependent on the qualifications and/or experience of the successful applicant. In addition, an annual vacation savings bonus up to R260 for married men and R130 for women and single men is payable, subject to Treasury regulations.

Application forms, further particulars of the post and information on pension, medical aid, staff bursary, housing loan and subsidy schemes, long leave conditions and travelling expenses on first appointment are obtainable from the Registrar, University of Natal, King George V Avenue, Durban, with whom applications, on the prescribed form, must be lodged not later than December 18, 1973, quoting Reference Advice 93/73. (1502)

Microbiologist

John Wyeth & Brother Limited, an expanding pharmaceutical company situated at Havant in Hampshire have an immediate vacancy for a Microbiologist in their Quality Control Laboratory.

The selected candidate should hold a B.Sc. Honours degree in Microbiology. This post calls for a high degree of initiative and would suit a young person looking for an opportunity to participate in the management of a major department.

Excellent terms and conditions, non-contributory pension and life assurance scheme in operation. Assistance with re-location expenses available.

Please write to Cameron Wolstenholme, Personnel Controller, John Wyeth & Brother Limited, Huntercombe Lane South, Taplow, Maidenhead, Berks, SL6 0PH.



(1525)



Wellcome

Scientific Administrator

Up to £4500

This is a new appointment in the Department of Virology at the Wellcome Research Laboratories at Beckenham in Kent. The post involves overall responsibility for the general administration of this large department, including budgeting, staff recruitment and control, financial records and procurement of supplies. Close liaison with service departments such as Finance, Engineering, Personnel and supplies will be necessary. Also involved will be the provision of technical and scientific support to the Departmental Quality Controller.

Candidates, probably aged 35 or over, must have extensive administrative experience. A scientific background probably in some area of biology would be a considerable advantage.

The Laboratories are situated in attractive parkland surroundings within easy reach of London and pleasant residential areas. Salary is negotiable, depending on age and experience, up to £4500. In addition the company offers excellent conditions of employment including pension and life assurance schemes.

Please write, giving brief details of qualifications and experience to

The Personnel Manager,
The Wellcome Research Laboratories,
Langley Court,
Beckenham BR3 3BS.

(1492)



UNIVERSITY OF LEICESTER DEPARTMENT OF GEOLOGY

Applications are invited for the post of ELECTRONICS TECHNICIAN, Grade 6, in the Geophysical section of the above department. The person appointed will be responsible for the maintenance and development of a wide range of laboratory and field equipment. He must be prepared to participate in field work programmes in the U.K. and overseas. A sound knowledge of electronics is essential and familiarity with Geophysical equipment would be an advantage. Supervision of and liaison with other technicians essential and some administrative duties are involved.

Minimum qualifications: H.N.C. or equivalent with 10 or more years' experience in related fields. Salary within the range £2,370 to £2,874. Applications should be made direct to the Chief Technician, Department of Geology, University of Leicester, University Road, Leicester LE1 7RH, giving full details of qualifications, experience, age and the names of two referees by November 30, 1973. (1490)

RESEARCH ASSISTANT UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL

Graduate with biochemical and biological background required for research involving cell culture and amino acid analysis in the study of inherited disease. Post tenable from January 1, 1974, for 1 year in the first instance with possible extension for a further 2 years. Salary scale £1,470 to £1,704 plus £126 London allowance, starting point according to experience. Enquiries to Dr. D. P. Brenton, Department of Human Metabolism, U.C.H. Medical School, University Street, London WC1E 6JJ. Telephone 01-387 9300, ext. 166. (1491)

UNIVERSITY OF ADELAIDE PROFESSOR OF ZOOLOGY

Applications from scholars with interests in any field of zoology for appointment in succession to Professor H. G. Andrewartha. The Professor will be Chairman of the Department for an initial term of five years when the position of the Chairmanship will be reviewed.

SALARY: \$A19,102 a year with superannuation on the F.S.S.U. basis.

FURTHER INFORMATION: Potential candidates are invited to obtain from the Secretary-General, Association of Commonwealth Universities (Appus.), 36 Gordon Square, London WC1H 0PF, or from the Registrar of the University, a Statement about the Chair and formal terms of appointment. Any further information desired may be obtained on request to the Registrar.

APPLICATIONS (in duplicate) giving the particulars listed in paragraph 9 of the Statement should reach the Registrar of the University, G.P.O. Box 498, Adelaide, South Australia, 5001, not later than December 15, 1973. (1484)

WESTFIELD COLLEGE (UNIVERSITY OF LONDON) ELECTRON MICROSCOPE UNIT

requires a TECHNICIAN GRADE 5 to take charge of the day-to-day running of the Electron Microscope suite and also to take an active part in training Postgraduates in Electron Micrography. The salary will be on the scale £2,007 to £2,382 plus London Allowance per annum. Applicants should hold an I.S.T. diploma in Electron Micrography and be able to use the AG1.801B microscope. Applicants without this qualification but willing to undergo training will also be considered but will be appointed on a lower grade.

Applications, giving full details and the names of two referees, should be sent to the Personnel Officer (N), Westfield College, Kidderpore Avenue, Hampstead, London NW3 7ST, by November 20, 1973. (1451)

UNIVERSITY OF LEICESTER DEPARTMENT OF PHYSIOLOGY LECTURER

Applications are invited for the post of LECTURER in the Department of Physiology (Head of Department, Professor R. Whittam, F.R.S.). An interest in teaching medical students is essential, and possession of a medical qualification desirable, but other suitably qualified applicants will be seriously considered. There are excellent research facilities.

Initial salary, dependent on qualifications and experience, within the scale £1,929 to £4,548 a year, with F.S.S.U. membership.

Further particulars from the Registrar, to whom applications should be sent by December 11. (1422)

ROYAL POSTGRADUATE MEDICAL SCHOOL. GRADUATE SCIENTIFIC OFFICER/TECHNICIAN required in Immunoassay Laboratory of the Endocrine Unit. Candidates should possess good biochemical and isotope qualifications and laboratory experience, preferably in a similar post. Salary according to qualifications and experience in range £1,600 to £2,300.—Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, W12 0HS, quoting Refer-

RESEARCH CHEMIST —Radiochemicals

The Union International Co. Ltd. wishes to engage a young Research Chemist, aged about 28/30, for the Radiochemical Section at the St. Albans Research Centre.

Experience in synthetic radiochemical techniques is essential, and candidates should be sufficiently well qualified and mature to justify appointment as Radiological Safety Officer.

The bench work will primarily involve the preparation of labelled bile acids and sterols and some experience of steroid synthesis would, therefore, be very desirable.

The salary is negotiable according to qualifications and experience, and there is a Contributory Pension Scheme. Some assistance would be given for re-location.

Applications, giving full personal and career details, should be sent to the Staff Manager (AD 5765), 14 West Smithfield, London, E.C.1.

(1507)

UNIVERSITY OF NATAL DEPARTMENT OF GEOLOGY, PIETERMARITZBURG

Applications are invited from suitably qualified persons for appointment to the post of

LECTURER OR JUNIOR LECTURER

The salary scales attached to the post are:

R4,800 by R300 to R6,900 per annum
R3,600 by R150 to R4,650 per annum

plus 15 per cent pensionable allowance on basic salary.

The commencing salary notch will be dependent on the qualifications and/or experience of the successful applicant. In addition, an annual vacation savings bonus up to R260 for married men and R130 for women and single men is payable, subject to Treasury regulations.

Application forms, further particulars of the post and information on pension, medical aid, staff bursary, housing loan and subsidy schemes, long leave conditions and travelling expenses on first appointment are obtainable from the Registrar, University of Natal, King George V Avenue, Durban, with whom applications, on the prescribed form, must be lodged not later than December 18, 1973, quoting Reference Advice 94/73.

(1501)

M.R.C. CLINICAL RESEARCH CENTRE (NORTHWICK PARK HOSPITAL) WATFORD ROAD, HARROW MIDDLESEX HA1 3UJ

Applications are invited for the post of RESEARCH ASSISTANT to Sir Peter Medawar, joining a small group of workers mainly studying transplantation and tumour immunity. Salary according to experience and qualifications. F.S.S.U. benefits.

Applications by November 30 to Sir Peter Medawar, from whom further particulars may be obtained. Ref. G1. (1506)

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING (UNIVERSITY OF READING) BACTERIOLOGY DEPARTMENT

A SUPERVISOR is required for a section responsible for preparation of bacteriological media. Applicants should have had sound training in chemistry or bacteriology.

An appropriate degree, H.N.D., H.N.C., or equivalent is required. The appointment will be in the Scientific Officer grade within a scale of £1,318 to £2,177 per annum according to qualifications and experience. Superannuation, with an allowance to offset contributions. Apply on forms obtainable from the Secretary, National Institute for Research in Dairying, Shinfield, Reading RG2 9AT. Quote reference 73/46. (1471)

UNIVERSITY OF KEELE DEPARTMENT OF PHYSICS

Applications are invited for the post of LECTURER tenable from October 1, 1974, to take part in the establishment of ELECTRONICS as a Principal undergraduate course. Experience in an applied area of electronics (e.g. in the telecommunications industry or in medical electronics) could be an advantage. Salary scale: Lecturer, £1,929 to £4,548. Further particulars and application forms from the Registrar, The University, Keele, Staffs, ST5 5BG, to whom they should be returned by January 8, 1974.

(1470)

RESEARCH TECHNICIAN

required to assist with a project involving Genetics, Biochemistry and Virology in the Department of Plant Biology and Microbiology. Salary (grade 2B) £1,524 by £54 to £1,794 per annum plus London Weighting £175 per annum. Five-day week. Five weeks (in total) annual leave. Letters only to Assistant Secretary (Establishment) RT/DH, Queen Mary College, Mile End Road, London E1 4NS, stating age, experience, qualifications and present work. Closing date November 10, 1973. (1485)

TECHNICIANS (2) REQUIRED IN BACTERIOLOGY DEPARTMENT for research with group investigating immune defences to bacterial infections. Salary according to age, experience and qualifications within scale £1,440/£2,292 per annum plus £126 per annum L.W.—Apply, The Secretary, St. Mary's Hospital Medical School, Paddington, W2 1PG. (1455)

FELLOWSHIPS AND STUDENTSHIPS

UNIVERSITY OF MELBOURNE JUNIOR RESEARCH FELLOW IN MARINE BACTERIOLOGY in the SCHOOL OF MICROBIOLOGY

Applications are invited for this position.

QUALIFICATIONS: The successful applicant should hold a Ph.D., have had research experience in marine or aquatic bacteriology, and be capable of independent research.

DUTIES: The Fisheries and Wildlife Department of the State of Victoria is co-ordinating a Pollution Survey of Port Phillip Bay. The Junior Research Fellow will study the bacterial flora of different representative environments in the Bay, to evaluate the effects of current practices of water management. These results will be co-ordinated by the Fisheries Department with studies of other parameters and used to construct a mathematical model of the Bay. The bacteriological research will be done in the School of Microbiology, and technical assistance will be provided; facilities for field work will be provided through the Fisheries and Wildlife Department.

SALARY: \$A7,556 in the first instance, with annual increments to \$A8,128. Limited assistance is available for travel to Australia for an overseas applicant.

The successful applicant would be required to begin duties in January 1974 and the grant is available for 3 years from that date. Further information can be obtained from Dr. N. F. Millis, School of Microbiology, University of Melbourne, Parkville 3052, Victoria, Australia.

Details of application procedure are available from the Registrar, University of Melbourne, Parkville 3052, Victoria, Australia. Applications, referring to Position No. B/2/73 and including the names of at least two referees, should be addressed to the Registrar and close on December 5, 1973. (1426)

UNIVERSITY OF BIRMINGHAM DEPARTMENT OF CLINICAL CHEMISTRY

Applications are invited from BIOCHEMISTS, preferably post-doctoral, for the post of RESEARCH FELLOW/ASSOCIATE to investigate the control of protein synthesis in human and animal tissue by hormones and other agents. The project is supported by a grant from the M.R.C.

Salary in the range £1,569 to £2,718, depending on qualifications, age and experience, plus F.S.S.U.

Further particulars may be obtained from Dr. D. R. London, Queen Elizabeth Hospital, Birmingham B15 2TH, to whom applications (3 copies), naming three referees, should be sent by November 30, 1973. (1479)

UNIVERSITY OF GLASGOW POST-DOCTORAL RESEARCH FELLOWSHIP IN BIO-ORGANIC CHEMISTRY

Applications are invited from post-doctoral bio-organic chemists for a research position (tenure 1 to 3 years) under an M.R.C. project grant to Drs. C. J. W. Brooks (Chemistry) and W. A. Harland (Pathology) for biochemical studies of human atherosclerosis. The research depends on the refined use of modern chromatographic techniques. Experience in lipid or sterol chemistry, and in micro-analytical methods, would be advantageous. The post will fall vacant on December 1, 1973, and the initial salary will be in the range £1,929 to £2,223 per annum for suitably qualified applicants.

Applications, with curriculum vitae, citing two referees, should be sent to Dr. C. J. W. Brooks, Chemistry Department, The University, Glasgow G12 8QQ. In reply please quote Ref. 3381M. (1481)

THREE POST-DOCTORAL FELLOWSHIPS IN THE EARTH AND PLANETARY SCIENCES

The Lamont-Doherty Geological Observatory of Columbia University invites scientists interested in any field of the earth and planetary sciences to apply for the following Fellowships.

Two Post-Doctoral Fellowships, each awarded for a period of one year (extendable to two years in special instances) beginning in September, 1974, with a stipend of \$12,000 per annum. One Senior Post-Doctoral Fellowship, the stipend and term of the award to be arranged to suit the special requirements of the successful applicant. Completed applications are to be returned by February 15. Announcements will be made March 31.

Application forms may be obtained by writing to the Director, Lamont-Doherty Geological Observatory, Palisades, New York 10964. (1473)

THE UNIVERSITY OF SHEFFIELD

POSTDOCTORAL RESEARCH FELLOWSHIP

Department of Chemical Engineering and Fuel Technology

Applications are invited for a Postdoctoral Fellowship financed by an industrially sponsored grant to carry out research on ignition in gases containing spontaneously flammable substances. The appointment will be for one year starting as soon as possible.

Details from Dr A. N. Hayhurst, Department of Chemical Engineering and Fuel Technology, University of Sheffield, Mappin Street, Sheffield S1 3JD. Please quote Ref. R89/G. (1460)

KENT EDUCATION COMMITTEE MEDWAY AND MAIDSTONE COLLEGE OF TECHNOLOGY

SCIENCE DEPARTMENT

Applications are invited for the post of

POST-DOCTORAL RESEARCH FELLOW

to work on the surface properties of manganese dioxide. The project will involve the use of radioactive isotopes and high vacuum techniques and will be carried out in new, well-equipped laboratories. Experience in surface studies of powders is desirable.

The appointment, in the first instance, will be for two years with a possible extension to a third year; and the fellow appointed may be required to teach up to six hours per week.

Commencing salary: £1,660 per annum.

Applications, including curriculum vitae, to the Principal, Medway and Maidstone College of Technology, Horsted, Maidstone Road, Chatham, Kent. (1464)

UNIVERSITY OF GLASGOW DEPARTMENT OF NATURAL PHILOSOPHY RESEARCH FELLOWSHIP SOLID STATE PHYSICS GROUP

A post-doctoral research fellow is required to join a group concerned with structural studies of the surface of liquids by high energy reflection electron diffraction. At a later date this work may be extended to investigations of solid state surface phenomena. Experience of U.H.V. and/or electron diffraction methods would be desirable but not essential.

Salary scale for the post will normally be within the range £1,900 to £2,500 per annum, according to age and experience. Tenure two years on appointment, with possible renewal for a further year. F.S.S.U. benefits.

Applications, stating age, academic qualifications, research experience and the names of two referees, should be submitted not later than November 30, 1973, to Professor R. P. Ferrier, Department of Natural Philosophy, University of Glasgow, Glasgow G12 8QQ. In reply please quote Ref. 3380M. (1480)

UNIVERSITY OF NEWCASTLE UPON TYNE RIDLEY FELLOWSHIP IN AIR AND WATER POLLUTION DEPARTMENT OF CIVIL ENGINEERING

Applications are invited, from persons who have shown themselves able to carry out original research, for the Ridley Fellowship in Air and Water Pollution tenable in the Public Health Engineering Division of the Civil Engineering Department. The Fellowship is financed by the British Steel Corporation to promote research on some aspect of air and water pollution. Applicants should normally have a higher degree (preferably Ph.D.) in a relevant branch of Science or Engineering.

The normal tenure of the Fellowship will be three years from October 1974 (or such earlier date as may be arranged). The stipend for the first year of the Fellowship will be £1,929, for the second year £2,058 and for the third year £2,223 (plus F.S.S.U.).

Further particulars and application forms (which must be returned by December 31, 1973) may be obtained from the Registrar, University of Newcastle upon Tyne, 6 Kensington Terrace, Newcastle upon Tyne NE1 7RU. (1468)

GRANTS & SCHOLARSHIPS

UNIVERSITY OF NEWCASTLE UPON TYNE DEPARTMENT OF CHEMICAL ENGINEERING ESSO RESEARCH STUDENTSHIP

Applications are invited from graduates in pure or applied science for the Esso Research Studentship, of the value of £695 a year with remission of certain fees, tenable in the Department of Chemical Engineering. The person appointed will study the effects of electric fields upon suspensions of particles and may register for a higher degree. Applications, including a curriculum vitae and the names and addresses of two referees, should be sent to Professor J. D. Thornton, Department of Chemical Engineering, University of Newcastle upon Tyne, Merz Court, Claremont Road, Newcastle upon Tyne NE1 7RU. (1469)

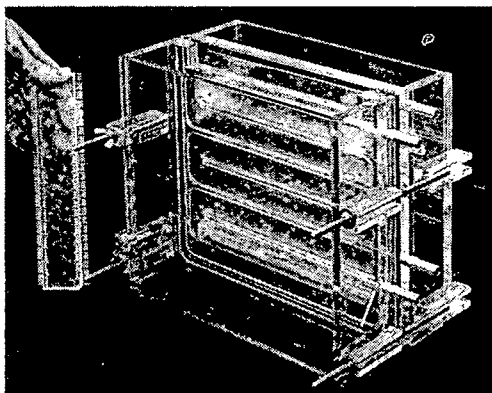
LECTURES AND COURSES

UNIVERSITY OF LONDON: A COURSE OF two lectures entitled "Brown Adipose Tissue: A Source of Extra Heat Production" will be delivered by Professor Olov Lindberg (Stockholm) at 5.30 p.m. on November 20 and 22 at University College, Anatomy Lecture Theatre, Gower Street, W.C.1. Admission free, without ticket.—Academic Registrar. (1466)

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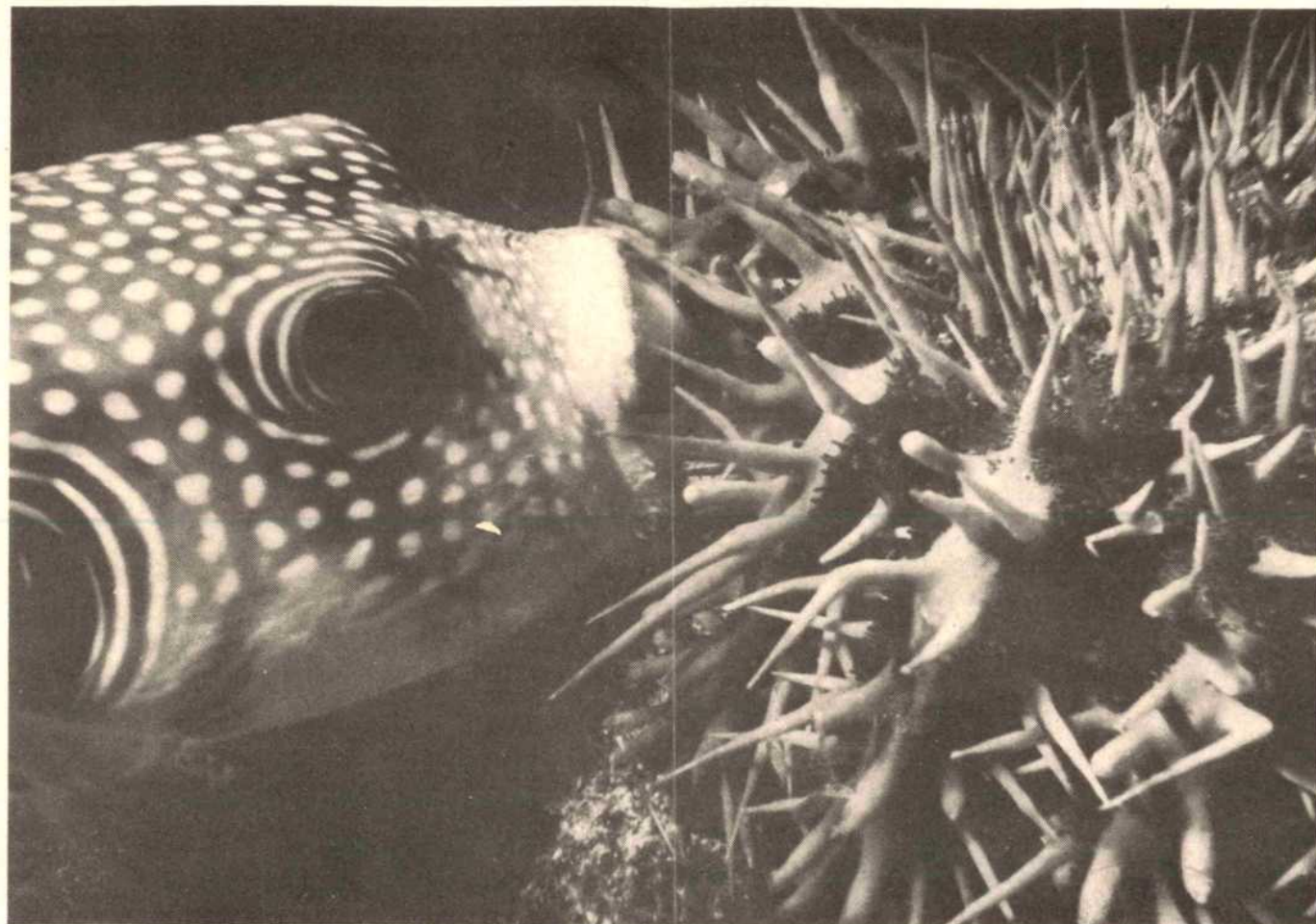
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Contents: Electron microscopy of nucleic acid molecules. Renaturation of DNA in the absence and in the presence of Cu^{++} ions. Interactions in nucleic acids. The polymer and salt induced condensation of DNA. The interactions of nucleotides with bovine pancreatic ribonuclease. The measurement of radiation-induced strand breaks in the DNA of mammalian cells. Stability and evolution of DNA from the point of view of molecular radiobiology. Author index. Subject index.

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	Page		Page
A Medal-seeker's Guide	113	Geophysics—Iceland mantle plume—SCHILLING (Rhode Island)	141
Analysis of Cause—Long Cut to Prevention?	114	Diamond synthesis—Galimov's cavitation hypothesis refuted—FRANK, LANG (Bristol) and MOORE (Royal Holloway College, London)	143
NEWS			
Slower and Cooler in the United States/Environment/South east Asia/OTA/Short Notes	116	Biological Sciences	
NEWS AND VIEWS			
Changing View of Operator-Repressor Interactions/Defence Mechanisms in Fish/Foetal Abnormalities/Astronomy/Population Ecology/Air Pollution/Burrowing Animals/Gravitation/Nuclear Physics/Palaeomagnetism/Chemistry	119	Cold therapy—A substituted guanidine with high activity <i>in vitro</i> against rhinoviruses — BUCKNALL, SWALLOW, MOORES and HARRAD (ICI Pharmaceuticals Division, Macclesfield)	144
ARTICLES			
Evolution of Insect Wings and Flight—WIGGLESWORTH (Cambridge)	127	C-reactive protein — Precipitins in plaice — BALDO (Cardiothoracic Institute, London) and FLETCHER (NERC Institute of Marine Biochemistry, Aberdeen)	145
Atmosphere—Diurnal variations in NO ₂ —BREWER, McELROY (Toronto) and KERR (Atmospheric Environment Service, Downsview, Ontario)	129	Anti-alloantibodies—Inhibition of local graft-versus-host reaction—BINZ, LINDENMANN (Zürich) and WIGZELL (Karolinska Institute, Stockholm)	146
Gene control—Structure of the λ operators—MANIATIS and PTASHNE (Harvard)	133	Nucleolus organisers—Technique for differential staining in mammalian chromosomes—MATSUI and SASAKI (Hokkaido)	148
LETTERS TO NATURE			
Physical Sciences			
Gamma-ray astronomy—Deuterium formation and the 1 MeV excess—LEVENTHAL (Bell Laboratories)	136	Chromosome staining—Why centric regions of quinacrine-treated mouse chromosomes show diminished fluorescence—WEISBLUM (Wisconsin)	150
Pollution—Average trace element composition of low level marine atmospheric particulates—CHESTER and STONER (Liverpool)	138	Mouse retina—Cytosine arabinoside and rosette formation in mouse retina—SHIMADA, WAKAIZUMI, KASUBUCHI, KUSUNOKI and NAKAMURA (Kyoto)	151
Palaeoclimate—New indicator—KEANY (Rhode	139	Lymphocyte receptors—Modulation of redistribution by con A, anti-mitotic agents and alterations of pH—YAHARA and EDELMAN (Rockefeller)	152

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 123 to 124

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	Page
Bacterial age —Crossbands of <i>Caulobacter crescentus</i> stalks serve as indicators of cell age—STALEY and JORDAN (Washington, Seattle)	155
Synaptic transmission —Histamine H ₁ - and H ₂ -receptors at a ganglionic synapse—BRIMBLE and WALLIS (Cardiff)	156
Insulin —Role of insulin as a 'permissive' hormone in mammary gland development—MUKHERJEE, WASHBURN and BANERJEE (Nebraska)	159
Pyran copolymer —Effect of molecular weight on biological activity—BRESLOW, EDWARDS and NEWBURG (Hercules Incorporated, Wilmington)	160
Malaria —Injection of malaria infected erythrocytes into rabbit pre-optic nuclei induces hyperthermia—ORSAY and HEATH (Illinois)	162
Kidney transplants —Rejection of first graft later in blood group O recipients than in others—JOYSEY, EVANS, HERBERTSON (Addenbrooke's Hospital, Cambridge) and ROGER (Cambridge)	163
Fluoride —Effect of sodium fluoride on regeneration in the rabbit ear—JOSEPH and TYDD (Guy's Hospital Medical School)	165
Retinal —Isomerisation of the visual chromophore all- <i>trans</i> to 11- <i>cis</i> retinal—O'LEARY, DUKE and EILERS (Oxford)	166
Crown-of-thorns starfish —Formation and breakdown of aggregations of the animal—ORMOND, CAMPBELL, HEAD, MOORE, RAINBOW and SAUNDERS (Cambridge and Coral Starfish Research Group, Sudan)	167
Insecticides —Modifications of pyrethroid structure give increased stability in light without loss of insecticidal activity—ELLIOTT, FARNHAM, JANES, NEEDHAM, PULMAN and STEVENSON (Rothamsted Experimental Station, Harpenden)	169

BOOK REVIEWS

	Page
From Stonehenge to Modern Cosmology, Fred Hoyle (HALTON ARP)	171
The Time of the Buffalo, Tom McHugh and Victoria Hobson (G. MALCOLM LEWIS)	171
The Universities and British Industry, 1850-1970, Michael Sanderson (D. S. L. CARDWELL)	172
Geology of the Country around Royal Tunbridge Wells, C. R. Bristow and R. A. Bazley (P. F. RAWSON)	173
Forces and Particles: An Outline of the Principles of Classical Physics, A. B. Pippard (W. COCHRAN)	173
Flight and Nature, M. W. Saunders (R. H. J. BROWN)	173
Problems of Heuristics, V. N. Pushkin (editor) (H. C. LONGUET-HIGGINS)	174
Medicine and Society, H. Miller (DAVID DAVIES)	174
Scientific Allocation of Water Resources: Water Resources Development and Utilization—A Rational Approach, Nathan Buras (T. O'DONNELL)	174
Mode of Action of Herbicides, Floyd M. Ashton and Alden S. Crafts (P. W. BRIAN)	175
The Water's Edge: Critical Problems of the Coastal Zone B. H. Ketchum (editor) (G. HOWELLS)	175
The Wasps, H. E. Evans and M. J. W. Eberhard (O. W. RICHARDS)	176
Motile Muscle and Cell Models, N. I. Arronet (E. W. TAYLOR)	176

CORRESPONDENCE

Smoking and Pregnancy (P. R. J. Burch; Richard J. Hickey, David E. Boyce, Richard C. Clelland, Evelyn B. Harner)	177
--	-----

Next Monday's issue will include

- Solar neutrinos**—More possible mechanisms for producing a low flux—DEMARQUE, MENGEL and SWEIGART (Yale)
- X-ray astronomy**—A steady energy source in Her X-1?—AVNI, BAHCALL, JOSS (Institute for Advanced Study, Princeton), BAHCALL (Princeton Observatory), LAMB, PETHICK and PINES (Illinois)
- Cosmology**—Effect of a local absorber in absorber theory—PEGG (James Cook)
- Physical chemistry**—Anion conductivity and disorder in lead fluoride—DERRINGTON and O'KEEFE (Arizona State)

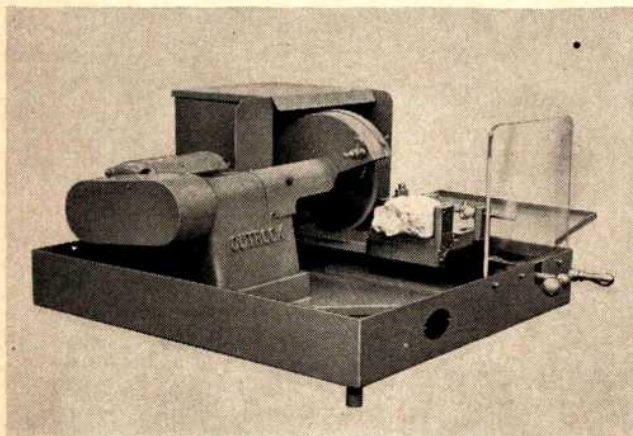
Next Wednesday's issue will include

- Threonine deaminase**—Role of the regulation of isoleucine and valine biosynthesis—LEVINTHAL, WILLIAMS, LEVINTHAL and UMBARGER (Purdue)
- RNA polymerases**—Yeast nuclear RNA polymerases I and II are immunologically related—HILDEBRANDT, SEBASTIAN and HALVORSON (Brandeis)
- Steroid hormones**—Synergistic effects of oestrogen and progesterone on oromucoid and conalbumin mRNA synthesis in chick oviduct—PALMITER and SMITH (Searle Laboratories, High Wycombe)
- Spina bifida**—An antenatal diagnosis in the Lewis rat—MACRI, EVANS (Nassau County Medical Center New York) and JOSHI (Downstate Medical Center, New York)



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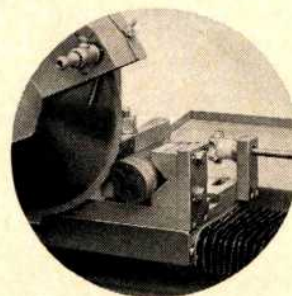
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A Medal-seeker's Guide

ALL that most scientists get for their hard work is a pay-packet and a vague feeling of satisfaction that one or two of nature's secrets have revealed themselves. Higher rewards, however, are available—medals and prizes. Since the cash is often not insignificant, we provide as a service to our readers a guide to landing some of Britain's plum rewards that they may have overlooked or thought inaccessible. There are no preliminary qualifications and in general the nationality of potential recipients is not taken into account in making awards. The selection of winners is entrusted to the Royal Society whose yearbook provides our information. As *Nature* goes to press, this year's winners are announced, so there are twelve months to make an impact before the next award. The most recent winners are not included in the statistics, which cover the last twenty years and may be helpful as a guide to prospects.

Copley Medal, 1731, silver-gilt. From legacy of Sir Godfrey Copley, Bt., F.R.S. (1653–1709). Annual. £100 added. An additional £1,000 comes from a Jaffé prize. Nobel laureates will recall that they are not eligible for Jaffé prizes, but for them £1,000 is available from 'another source'.

Given annually to the author of research published by the Society deemed 'deserving of that honour'. In the middle of the nineteenth century the medal was "recognized as the 'palm and laurel' of science" (*Nature*, 174, 1034; 1954) and thirty-two of fifty awards between 1851 and 1900 went to foreigners.

To two Foreign Members in the last twenty years, otherwise to Fellows of the Royal Society, generally of twenty years' standing.

Rumford Medal, 1800, silver-gilt. By Count Rumford, F.R.S. Biennial. £200 added.

Given to the author of the most important discovery in any part of Europe in Heat or Light.

To a Dutchman in 1964, otherwise to Fellows on each occasion in the last twenty years.

Royal Medals, 1825 and 1965, gold. Three available. Annual. No money.

Given for the most important contributions in pure and applied science published in Her Majesty's Dominions.

Of forty-eight recipients, forty-six were already Fellows. Helpful to have been one for at least ten years.

Davy Medal, 1877, bronze. Of obscure origin believed to be connected with pawning of Sir Humphry Davy's tableware. Annual. £200 added.

Given for the most important discovery in chemistry in Europe or Anglo-America.

Not much good chemistry outside Britain these days. Of last twenty recipients, one Swiss, two American and seventeen Fellows of the Royal Society.

Darwin Medal, 1890, silver. Biennial. £200 added.

Given for work of acknowledged distinction in the field in which Charles Darwin laboured.

No limitation of nationality or sex. One Foreign Member, nine Fellows in last ten awards. All male.

Buchanan Medal, 1897, silver-gilt. Quinquennial. £200 added.

Given for distinguished work in Hygienic Science or Practice.

No limitation of nationality or sex. Two of last four winners were not Fellows, but all were male.

Sylvester Medal, 1901, bronze. Triennial. £200 added.

For the encouragement of Mathematical Research, irrespective of nationality (sic).

Last six recipients should have needed no encouragement to carry on, as they had been Fellows for on average twenty years.

Hughes Medal, 1902, silver-gilt. Given by Professor David E. Hughes, F.R.S. Annual. £200 added.

Given for original research, particularly in Electricity and Magnetism.

No restriction on nationality or sex, but the last twenty recipients have all been male Fellows.

Leverhulme Medal, 1960, gold. To mark the tercentenary of the Society. Triennial. £500 added.

Given for the most significant contribution in chemistry or engineering.

In 1966, Sir Alec Issigonis won this medal before being made a Fellow.

Mullard Medal, 1967, gold. Annual. £1,000 added.

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100 Years Ago



WE learn from the Journal of the Society of Arts, that one of the first results in the rise of the price of coal has been the formation of a company in France, whose object is to utilise the power of the ocean tides on the French coast by proper machinery. The first experiment is to be made at St. Malo, where the tide rises nearly 80 ft., and overflows many square miles of flats.

From *Nature*, 9, 54, November 20, 1873.

Analysis of Cause—Long Cut to Prevention?

"Abatement is the aim of medicine . . . even the concept of causation can, on occasions, be dispensed with in considering abatement strategies."

Dr J. H. Renwick of the London School of Hygiene and Tropical Medicine urges the need for more emphasis on preventative thinking in framing hypotheses in medical science.

ALTHOUGH in biomedical research prevention of a disease is customarily considered complementary to its cause, most of the scientific working hypotheses are framed around testing the supposed cause directly. In some circumstances, however, there are advantages in framing hypotheses around prevention.

I shall consider first the circumstances in which the classical causal hypothesis is more or less adequate. These arise either when a disease situation occurs naturally that superficially resembles a laboratory experiment or when a true experiment is possible in an animal that is acceptable as a valid analogue of man.

The thalidomide incident is an example of the natural or at least unplanned experiment. When thalidomide was taken by pregnant women and a defined range of otherwise rare malformations was observed in many of their offspring but not in the offspring of other women, the hypothesis was

proposed that thalidomide was at least a contributory cause of these malformations in humans. Indeed, for any new ailment (disease, malformation or injury), it is simple and effective to state a proposition in the causal mode. As in a classical experiment, a known background situation is modified and an effect produced.

An animal experiment with thalidomide would be an example of the other situation (of adequacy of a causal hypothesis) but only when the test animal is trusted as a valid analogue of man. Rhesus monkeys and certain marmosets are so trusted; the malformations produced in them by this drug are almost identical with those in man. A causal hypothesis even for man, being therefore indirectly testable, can usefully be proposed.

Need for Abative Hypotheses

The position is different for ailments to which man has been subject for a long time and for which no convincing animal analogue is available. Unfortunately, we are in the habit of constructing causal claims about even these ailments although the relevant experiments to test the claims directly would usually be unethical. The causal experiments are therefore impracticable except in imagination. In a 'thought experiment' of this sort, an artificial base-line for the population has to be created. In one example, it could involve the (imaginary) absence of refined sucrose. This basal situation would then be modified (in imagination) by the addition of sucrose and various alimentary disorders would ensue. Such at least is the experiment that seems to be suggested by a causal claim that sucrose is an important factor in the cause of colonic diverticulosis, for example. The hypothesis cannot be tested directly because it is nearly always unethical to increase the risk of ailment in a real experiment.

If we can overcome the habit of allowing cause to dominate our thinking, we have a very simple way of bypassing such a problem. This is to perform a real intervention experiment on a part of the population with its present, known burden of disease. This basal situation is then modified—by some procedure such as reduction of intake of refined sucrose. The degree of abate-

ment of the disease is then the outcome of the experiment. With such an experiment in mind, a preventative hypothesis can be formed that is in principle testable, and there are usually no major ethical objections to an experiment of this sort. Further, the statement can be framed briefly yet accurately in terms of deviation from the present state because the 'present state' is known widely enough for it to require, in many cases, no detailed description. Many intervention experiments of exactly this type are done. The change that I am suggesting is that they should be acknowledged as testing preventative statements and not causal ones.

Preventative statements, when confirmed, will sometimes summon up practical measures to control disease. Any such measure—it may be preventative or therapeutic or both—will be called 'abative' as its purpose is to produce some abatement of the ailment and of its burden to the individual and to society.

Non-reciprocal Relationship between Cause and Abative

Wherever a necessary-and-sufficient abative measure exists there must, in principle, be a corresponding necessary-and-sufficient cause and *vice versa*. The search for cause or abative then comes to much the same task. But the relationship between cause and abative is not always so exactly reciprocal. For instance, a sufficient abative is one that removes a necessary cause. A somewhat oversimplified example of a 'sufficient abative' would be the banning of rye cultivation to prevent poisoning by the ergot fungus, for which rye is the preferred host. The corresponding causal statement is that rye is the 'necessary cause' of ergot poisoning. As in this example, so in general—an abative measure that has the property of sufficiency but not of necessity is the counterpart of a cause that is necessary but not sufficient.

The degree of reciprocity is also limited in a more subjective way. Even though abatatives, like causes, do interact, the percentage abatement of a disease incidence by a single manipulation is an unambiguous and complete concept. By contrast, the concept of the percentage effect of a single cause is more likely to be misleading unless the inter-

actions with other causes are fully specified. Specifying these interactions by the disclaimer—other things being equal—is rarely adequate.

Few such difficulties apply to statements or hypotheses on abatement. The effects of single causes or abatements are best expressed as percentage change from the initial situation. The effects (causal or abative) may sum to several times the incidence of the disease. This is not awkward if it is abative effects that are being summed since each is operative only potentially and mainly in the future. We are not surprised at the existence of alternative means of prevention nor at the possibility of their interacting, so when the sum exceeds 100% effectiveness, we are not disturbed. But there is a seeming absurdity in the statement, say, that 50% of the present incidence of a disease is caused by each of three factors, x , y , z . For the claim to be explicit, interactions or options must be invoked because, obviously, the realised effect of the three factors combined does not exceed the present overall incidence.

As already noted, intervention studies of abative measures are already an established part of epidemiological practice. For example, there have been non-smoking studies, breathalyser studies, and, on the positive side, fluoridation studies. But the conceptual framework has not been adequately spelled out to my knowledge. In some intervention studies, by a curious inversion, the investigators even imply that causes are being studied rather than abatements. The distinction is worth making as it reflects a difference. Abatement is the aim of medicine; the study of causation of an ailment, say, in experimental animals, is frequently a useful intermediate but may not be an essential one in all cases. Even the very concept of causation can, on occasion, be dispensed with in considering abatement strategies.

Remaining Problem Diseases are a Selected Sample

I suggest that if neither causes nor abatements are yet known—and I shall call such an ailment a problem ailment—causation is probably complex. The more complex the causation, the more likely it is to be currently unknown. In tackling such a problem ailment, then, we would be wise to turn at least some of our attention from causes to abatements. For example, the causal mechanism of carcinoma of the colon is unknown and probably complex. From its geographical distribution the simple and testable abative measure of a high residue diet has been proposed. From past neglect, simple abatements like this

have not always been adequately excluded.

Advantages of Abative Statements

For old-established conditions, three major advantages of abative compared with causal statements have so far been mentioned—direct testability on the human species itself; expressibility in simpler terms; and the opportunity to include a quantitative component that expresses the percentage of prevention anticipated.

This last advantage is well illustrated in the case of road accidents. We should like to make statements such as "20% of accidents in the United Kingdom are caused by alcohol", but such statements are intrinsically misleading because of the interactions: practically no cause operates in isolation. An abative statement that the introduction of the breathalyser laws in the United Kingdom reduced the accident rate by a certain percentage is simpler and open to a smaller range of interpretations.

This example introduces another important advantage of abative propositions. They are directly relevant to the achievement of human goals such as the partial prevention of accidents, and so are directly relevant to decision making in public and private life. The quantitative aspect is the most important in this context, as the predicted advantage has to be balanced against the cost of introducing the abative measure.

It is at least arguable that if the observed association between smoking and lung cancer had led to an abative rather than a causal claim, society's 20 yr delay in taking action would have been shorter. The claim would have been directly confirmed by the results now available of non-smoking intervention studies and the question of the identification of the presumed carcinogen(s) could have been deferred. Further, the genetic red herring would have been more clearly recognised for what it is—a matter of intellectual interest but with little practical relevance, in this instance, in decision making.

Perspectives on Causation and Abatement

The properties of abative statements are so attractive that we need to ask why they are rarely made. After all, if prevention of disease is an aim of medicine, why have we departed so completely from the folklore mode of expression exemplified by 'an apple a day keeps the doctor away'? The historian might well find an influence of the philosophy of non-medical science—

the dominance of how (does it happen) over how not. Waddington in *The Scientific Attitude* roughly defined science as "the organised attempt of mankind to discover how things work as causal systems". Perhaps the absence of specific mention of abatement in such definitions has been taken to imply that abative statements are less scientific than causal ones, despite the fact that, for both types, the "criterion of truth is experimental" and objective.

Alternatively, did the current emphasis on causation spring from the need of the legal system to apportion blame? Or, equally plausibly, was the need to study epidemics more pressing than the need to study the less dramatic non-epidemic state? The manifest success of laboratory methodology in so many non-human fields undoubtedly played a large part in establishing the habit of thinking in the causal mode. We correctly believe that we have not understood anything at a fundamental level unless we have understood the mechanism of causation. And we often think (incorrectly) that such understanding is a prerequisite of wise action. Kant knew better—that "it is often necessary to make a decision on the basis of knowledge sufficient for action but insufficient to satisfy the intellect".

It is true, even today, that wise action can occasionally be based at least temporarily on empirical knowledge alone and there are many examples of this from the past. From the time of Admiral Wager, scurvy was controlled in the Navy by the provision of citrus fruits before ascorbic acid was known to be a vitamin. Penicillin was used effectively, even before its mode of action was understood; and tobacco avoidance dramatically reduces bronchocarcinoma incidences although we still do not know how.

Decision-making in medicine is more directly concerned with prevention and treatment rather than causation, so we should often express claims in terms of abatement rather than causation as at present. A few scientists disagree. They argue that causation and abatement are simply converse concepts and, at the same time, that one is scientific, the other empirical. Both arguments are rather shallow assessments. Abatement is not always the simple converse of causation. Further, an abative statement can be as scientific and testable experimentally as any other. It may even be just as possible to discover general laws concerning abatement as laws concerning causation.

Abative and causal hypotheses are not mutually exclusive. Indeed, there is a one-to-one relationship between them. The abative statement is usually simpler in practice. This is particularly true for complex problems. And most real-life problems are complex.

NEWS

Slower and Cooler in the United States

by our Washington Correspondent

IN the next few months, nearly every American is going to be brought face to face with the energy crisis, for it is now clear that there may be rationing of petrol and heating oil, closing of some schools and offices, shorter working hours and even a few cold homes. Apart from the inconvenience and upset that these situations will cause, their overall effect will be to force Americans to cut back on their use of energy—not just this winter, but permanently. And that will require some rather fundamental changes in a society that has been mindlessly consuming energy at a staggering rate.

Last week, President Nixon went on television to warn the country of the gravity of energy shortages that are likely to develop in the United States this winter, and to outline emergency measures that his Administration wants to take to deal with the situation. The reaction has been startling. Newspapers have been filled with little else—for a time the energy crisis even eclipsed Watergate as the focus of national attention—state governors have been announcing measures to curtail consumption of energy in their territories, and a few people have turned down their central heating. On Capitol Hill, committees have been stung into action and have passed legislation to give the President sweeping powers to force a reduction in the use of energy throughout the country. And the Stock Exchange has seen the biggest drop in share prices in 11 years.

The root cause of the impending shortages is that the growth in energy consumption in the United States has for years been outstripping the growth in supply. But the situation has been blown into crisis proportions by the embargo that Arab countries have placed on their oil exports to the United States, an action which will strip 2 million barrels of oil a day off the supply. The Arab cutoff, together with shortages that were developing in any case, could result in oil supplies falling short of demand by 17% when winter finally arrives. The problem, however, is that the shortages will not be evenly distributed, for it is predicted that the gap could reach an incredible 40% in the Northeast, an area which relies heavily on imported oil.

That is the prospect which caused President Nixon last week to deliver his third energy message to the American public so far this year. Unlike the pre-

vious messages, which have been concerned chiefly with increasing energy supply, and which have paid only scant lip service to the need for reducing demand, the latest effort was concerned almost exclusively with emergency measures that must be taken to decrease consumption of energy. The message came too late, and it was only forced by what President Nixon referred to as "the most acute shortages of energy since World War II", but nevertheless it represents a fundamental break with the Administration's previous attempts to deal with the energy crisis.

What Nixon is asking, in short, is for Congress to give him broad emergency powers to force people to curtail their energy appetites, and he is also appealing to the American public to act voluntarily.

Among the measures outlined in his message are the following:

- The Administration wants the power to order neon lights and ornamental lighting to be turned off, a measure which would have the welcome effect of getting rid of some of the neon nightmares that encircle so many American cities.

- President Nixon is requesting authority to force shops to close early, to require speed limits to be lowered on all roads, and to impose emergency taxes on consumption of natural gas and on excessive uses of electricity.

- He wants Congress to pass a bill authorising the use of daylight savings time (the equivalent of British Summer Time) throughout the year—a measure which could save up to 3% in electricity consumption, particularly in the northern areas which are most affected by lack of fuel.

- Finally, he is asking for broad authority to allow power plants to be exempt from air pollution regulations, so that they can burn coal and oil containing relatively large quantities of sulphur.

Those measures all require Congressional approval, but the Administration already has powers to force other changes, and it is using them. Regulations are being drawn up to prevent factories and power stations from switching from coal to oil, and the Administration is also putting pressure on electricity producers to convert power plants from oil to coal. The White House says that 46 plants can be converted within two months, at a saving of nearly half a million barrels of oil a day. The number of commercial jet flights in the United States has been reduced by the

Federal Aviation Administration, and Nixon decreed that thermostats be turned down in federal buildings. He also appealed for central heating to be turned down in private homes, for cars to be driven at speeds less than 50 m.p.h., for more use of mass transit, and for more car pooling.

Scarcely were the words of exhortation out of President Nixon's mouth when Congress was galvanised into unprecedented action. Senator Henry M. Jackson, chairman of the Senate Interior Committee and the most influential member of the Senate on energy matters, rammed a bill through his committee, after a day of hearings in a cool committee room, and the House Commerce Committee also expects to get a bill passed this week. Thus Congress is likely, by the end of next week, to have given President Nixon most of the powers he requested.

The emergency measures proposed by Nixon seem tougher, at least if implemented, than the British government's proposals announced on Tuesday in the face of a crisis exacerbated by a miners' overtime ban.

But will they be sufficient to cope with the situation? By all accounts they will not, and the Administration is developing plans to ration petrol and fuel oil if the need arises. For one thing, the measures announced last week will rely heavily on public cooperation and voluntary compliance, and for another, some of them have come too late to be effective. For example, the proposal to convert power plants from oil to coal—a fuel which the United States has in abundance—is likely to be stymied by the fact that coal production is already taking place at maximum capacity, and thus it is unlikely that coal output can be increased in time to meet a new surge in demand. Moreover, according to the White House's most optimistic forecasts, the proposals will cut demand for oil by some 2.3 million barrels a day, a figure which is well short of the predicted gap between supply and demand of three million barrels.

Thus, senior Administration officials are warning that it is likely that oil and gasoline rationing will have to be brought in before the winter has ended. Moreover, the problems will not disappear at least until the end of the 1970s when the Alaska pipeline will be bringing crude oil to the lower states. This winter is therefore likely to mark the end of an era of cheap, bountiful energy in the United States.

ENVIRONMENT

Environmental Protection

by our Washington Correspondent

THE House Appropriations Committee has handed both the Environmental Protection Agency and the National Academy of Sciences a political hot potato which could prove embarrassing. The committee passed a bill which includes \$5 million for the EPA to let a contract with the academy to carry out a massive study of the EPA's programmes and past decisions. That provision was eventually passed by the House of Representatives and the Senate, and it was signed into law at the end of last month. If the academy agrees to accept the contract, it will undertake one of the biggest and most difficult studies it has ever been involved with, and it will also run the risk of being used by hostile Congressmen as a weapon in their campaign to emasculate the EPA.

The appropriations bill itself carries the bare statement that \$5 million be provided for the academy to study the EPA, but the House appropriations committee report spells out the nature of the study in some detail. The committee suggests that the study should involve an estimate of the costs of pollution abatement over the next 10 years and that it should include an analysis of the costs and benefits of the pollution control programme—an analysis which should bring in social and economic factors.

The committee also propose that the academy be given the task of examining the costs and benefits of automobile emissions controls, the extent to which environmental regulations have contributed to the energy crisis, and the effect on agricultural productivity of various decisions to ban pesticides. Virtually every one of those topics has already been the subject of intensive study and heated debate, and there are many who find it difficult to see what new insight the academy might be able to bring to the matter.

Why was the provision put into the bill? The answer, in short, is that the EPA is unfortunate enough to have its budget scrutinised by the agriculture subcommittee of the House Appropriations Committee, and many powerful members of the subcommittee, being closely allied with farming interests, regard the EPA with about as much affection as they do the boll weevil. The chairman of the subcommittee, Jamie Whitten, a conservative Democrat from Mississippi, makes no attempt to conceal his contempt for the EPA. Last week he told the House of Representatives that the agency has contribu-

ted to the energy crisis, increased the costs of food production, increased the danger to human health by banning DDT, and put American agriculture at a competitive disadvantage.

Thus the committee is looking to the academy to provide intellectual support for its complaints about the EPA, which is an unenviable position for the academy and for the EPA to be placed in.

SOUTH EAST ASIA

North Vietnam Appeal

by our Washington Correspondent

THE Scientists' Institute for Public Information (SIPI), a public interest organisation, has launched an appeal in the scientific community for help in repairing some of the destruction caused by US bombs, herbicides, shells and other weapons in Southeast Asia. The immediate goal is to establish a Research Institute for Agricultural Botany in North Vietnam—a project which has been specifically requested by North Vietnamese scientists to help revegetate rural areas which are extensively littered with bomb craters.

According to Dr Barry Commoner, past president of SIPI, the appeal will serve the dual purpose of alerting US scientists to the post-war situation in North Vietnam and of informing the US public of the need to provide aid to all of Indochina. This is a promise which in fact was made by President Nixon during the cease-fire negotiations but which has since fallen into political disfavour.

The idea for the agricultural research institute stems from a visit to North Vietnam made in July this year by two American scientists with the support of SIPI. Dr E. W. Pfeiffer, a zoologist from the University of Montana, and Dr Arthur Westing, a botanist from Windham College, Vermont, returned with reports of devastation on a scale which Dr Westing said last week was "almost unbelievable". He said that they were rarely out of sight of bomb craters, even in the most rural areas of North Vietnam, and since more than 90% of the population is directly engaged in agriculture, Dr Westing pointed out that the greatest need for aid lies in rehabilitating the rural areas.

The SIPI appeal started this week with a letter sent by Dr Commoner and Dr Arthur Galston, professor of botany at Yale University, to some 10,000 scientists asking for aid in establishing the research institute, for scientific books and journals to be sent to North Vietnamese scientists and for equipment for the institute. Dr Galston said last week that \$100,000 will be enough to start the institute off, and that SIPI is hoping to get some of the money from

institutions and foundations. He reckons that sufficient cash and equipment should be available by April 1974 to send a small team of US scientists to North Vietnam to work in the research institute. In addition, SIPI has arranged to ship scientific books and journals to South Vietnam by way of Dr Philip Harvey, of St Stephen's Hospital in London.

OTA

Daddario Appointed

MR EMILIO Q. DADDARIO has, as expected, been appointed the first director of Congress's new Office of Technology Assessment. The appointment puts Daddario in charge of a body which he is largely responsible for setting up, and brings him back to Capitol Hill three years after he left the House of Representatives to make an unsuccessful bid for the governorship of Connecticut.

A lawyer by training, Daddario was elected to Congress in 1958, and in 1963 he became the first chairman of the subcommittee on Science, Research and Development. Under his stewardship, the subcommittee rapidly established itself as the focal point for discussion of science and technology policy issues in Congress. It also rather grotesquely revamped the National Science Foundation by making its top officials direct Presidential appointments and enabled the NSF to sponsor applied research. The subcommittee began hearings on research into environmental problems before the environmental bandwagon had even begun to move, and drew up the legislation which eventually led to the establishment of the Office of Technology Assessment.

Daddario's appointment was confirmed when the OTA board met early in November—its first meeting since the office finally got some funds to begin work (see *Nature*, 246, 6; 1973). Next step is to appoint a deputy director and an advisory council. The most likely candidate for deputy director is Daniel V. Simone, a former member of the defunct Office of Science and Technology, who is now on the staff of the NSF's Office of Science and Technology Policy. There should be little problem in finding good staff for the OTA—some 3,500 people have applied for jobs there, even though none has been formally advertised.

Short Notes

CSII on Ice

THE Centre for the Study of Industrial Innovation is in danger of dying from neglect. Negotiations between the centre's directors and the Cranfield Institute of Technology, which it was hoped would lead to the centre becoming a department of industrial innovation at the institute, have scarcely moved in the past nine months.

A recent meeting between Mr George Teeling-Smith, the centre's director, and Dr Henry Chilver, the Vice-Chancellor of Cranfield, means that discussions are still continuing, but the centre has effectively been out of operation since January of this year.

Mr Teeling-Smith said this week that it is "disappointing that it is taking so long" for any changes to take place. "We have lost so much impetus that effectively we will be starting from scratch again." At present CSII has nothing to do except sell back copies of its reports on industrial innovation, which include an assessment of the spin-off benefits from Concorde, an appraisal of the industrial research associations and the publication of the results of the Project Sappho studies on industrial innovation undertaken at the University of Sussex.

Dumping at Sea

A BILL to control dumping at sea has just been introduced to parliament. To date dumping has been limited by voluntary agreements between industry and government. Over the past seven years this has been quite effective but the bill will formalise the voluntary arrangement, making it necessary to acquire a licence to dump any material in the sea, and introducing heavy penalties for offences.

If the bill is passed Britain could be the seventh country to ratify its signature to the Oslo convention agreed in February 1972, which dealt with dumping in the north-eastern Atlantic. This convention requires ratification by seven countries to come into force. The bill will also enable Britain to ratify the London convention, concluded in December 1972, which was a global convention on similar lines to the Oslo convention. This requires ratification by fifteen countries to come into force, and Britain will probably be only the third country to ratify it. It is not, however, as immediately important to British fishing as the Oslo convention, which is concerned with the sea around the British Isles.

The basic determinant on which the decision to grant a licence will be based is the effect of the dumped material on fish. Certain substances which persist in the environment are blacklisted,

and licences for their dumping will never be granted. These include mercury, cadmium, and DDT. For dumping of other materials, including arsenic, lead and fluorides, a special licence is required, and the materials must be dumped in deep water, at least 150 nautical miles from land. Factors such as the concentration and form of the material and the area in which it is to be dumped will be taken into account in the issuing of all licences.

Dumping at sea is responsible for only 5-10% of shore-generated marine pollution. The main sources, streams and pipelines, are not affected by this bill, but will be dealt with in another bill to be published shortly, concerned with many forms of pollution including atmospheric and noise pollution. Neither does the present bill cover atomic waste, which was dealt with by the act of 1969, nor with pollution from ships, which was discussed last month in a convention in London.

Solar Energy in Australia

AUSTRALIA is expanding its interest in solar energy business with some enthusiasm. Last week a Solar Energy Studies Unit was formed by CSIRO under the direction of Mr R. N. Morse, formerly chief of the CSIRO Division of Mechanical Engineering, and immediate past president of the International Solar Energy Society.

CSIRO has had an interest in solar energy for almost twenty years, and solar heating of water is already in use to the extent of saving Australia 5,000 tonnes of coal a year. Solar heated air is also used in some industrial drying processes, while experimental timber drying kilns are already being tested.

The new unit will look at the most promising applications of solar energy for Australian conditions. Feasibility studies of short and long term projects will be undertaken, focusing current CSIRO fundamental work on solar energy collections, heat storage media, energy measurement and thermal transfer problems.

Mr W. L. Morrison, Australia's minister for science, announcing the appointment said that "the use of solar energy on a wide scale for domestic and industrial heating could help substantially to offset increased costs of fossil fuels in the future".

Developing Research

THE National Research Development Corporation is alive, well and even flourishing. This is the message contained in the corporation's annual report published last week (available free from NRDC, 66 Victoria Street, London, SW1).

The NRDC has come in for some criticism recently, particularly at the

hands of the Select Committee on Science and Technology which recommended that the corporation's structure needed "urgent financial review". This criticism was included in the select committee's report (published in September) on the closure of Tracked Hovercraft Limited, an NRDC subsidiary.

Dr Basil Bard, the corporation's managing director, said last week that the forecast for the future is encouraging with a net surplus for 1972-73 reported of £529,000 compared with £178,786 the previous year. The total income of the corporation went up from £7.4 million to £8.7 million.

One of the problems which the corporation is faced with, according to the report, is that of "maintaining in industry, in the universities and in other sources of invention, a knowledge of the corporation's existence and of the facilities it is able to provide for promoting innovation in industry".

Dr Bard said that in the past year uncertainty about the corporation's future had been replaced "by an increased awareness of the need for a body like the corporation, which has encouraged us in our belief that we have an important part to play in providing financial aid for the development and commercialisation of significant UK innovation". This, however, does not take any heed of the select committee's views.

Comet Kohoutek Disaster?

DR D. W. DEWHIRST of the University of Cambridge warned a meeting of the Royal Astronomical Society last week that members should be cautious in their public statements about Comet Kohoutek. Little is known about the factors that govern a comet's brightness, he said, and the prediction that Kohoutek will be a bright object in daylight may be over-optimistic. According to his calculations the brightest that the comet will be as viewed from Britain is magnitude -3 (on January 3) which is about as bright as Venus. Perhaps Dr Dewhirst has recalled that the failure of the Leonid meteor shower to live up to expectations in 1899 was described by the meteor scientist C. P. Olivier as "the worst blow ever suffered by astronomy in the eyes of the public".

More Mobility

SIR HERMAN BONDI's task force to encourage the mobility of scientists is nearing the end of its appointed task. Its report is being written at present and will be submitted to the Lord Privy Seal at the end of the year or in January.

There is no news of what the report contains but it is highly unlikely that the work started by the task force will be allowed to come to an end with the publication of the report in the Spring.

NEWS AND VIEWS

Changing View of Operator-Repressor Interactions

ONE of the most critical steps in the development of theories of gene control was the concept that some sequences of DNA may function not by their transcription into RNA and subsequent translation into protein sequences, but rather by serving as signals which are recognised by protein molecules acting as regulators or enzymes of gene expression. Elucidation of the mechanism of such protein-DNA interactions has become a principal aim of current research, in particular concerning the promoter sequences recognised by RNA polymerase and the operator sequences recognised by repressor proteins. The two systems which have proved particularly productive, the lactose operon of *Escherichia coli* and the early development of phage lambda, now seem likely to present very different pictures of repressor-operator interactions.

Operators have in general been thought of as rather short sequences of DNA; a consensus of opinion which is presently evolving is that they comprise, or at least include, symmetrical sequences of base pairs. A sequence of the order of twenty base pairs with features of symmetry seems, for example, to constitute the operator of the lactose operon. But the most recent work of Maniatis and Ptashne, reported on page 133 of this issue of *Nature*, replaces the idea of a single short sequence with the concept that in lambda the two operators may each comprise more complex structures, capable of recognising several repressor molecules.

The two lambda operators comprise sequences of DNA to which the lambda repressor protein binds to maintain the phage in an inactive state, by preventing transcription. Repressor binding to the 'left' operator prevents synthesis of the RNA corresponding to gene *N* immediately to the left of O_L and repressor binding to the 'right' operator similarly prevents transcription of gene *toI* lying immediately to the right of O_R . In the experiments which they now report, Maniatis and Ptashne take advantage of the techniques reported earlier this year by Pirrotta (*Nature new Biol.*, **244**, 13; 1973) for isolating the lambda operators. Radioactively-labelled lambda DNA, sonicated to yield fragments of molecular weight $3-6 \times 10^5$, is bound to the lambda repressor protein and, in several subsequent steps, the sequences of DNA not protected by the repressor are degraded with DNase and the operator sequences are retrieved by binding the repressor-operator complex to nitrocellulose filters. Since the yield of protected DNA is twice as great with wild type lambda DNA as with a mutant possessing only one operator, both of the operators of lambda can be isolated in this system.

In early experiments, the fragment of DNA protected by repressor corresponded to some twenty base pairs in length. This is much larger than had been anticipated, because in its active dimer form the repressor protein should cover only some ten to fifteen base pairs of DNA. That the additional length results from the ability of each operator to bind more than one repressor was shown by Maniatis and Ptashne earlier this year (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 1531; 1973), when they found that upon digesting lambda DNA with nuclease in the presence of

lambda repressor, the size of the protected fragments increases as the ratio of repressor to operator increases. The smallest fragment corresponds to a length of some thirty-five base pairs, the size then increasing with the repressor/operator ratio to 45, 65, 75, 85, 100 base pairs. By comparing the pyrimidine tract sequences obtained from the left operator, they were able to show that each increase in size of the protected fragment represents the addition of a short sequence to the fragment immediately preceding in the series. This suggests a model in which the operator consists of a sequence about thirty base pairs long which binds a dimer of repressor; following binding to this primary site, additional monomers of repressor may add to sequences about fifteen base pairs long adjacent to the primary sequence. A further indication of the complexity of the operator-repressor interaction in lambda is provided by the observation that, although displaying similar hierarchical structures, the left and right operators constitute different sequences—they generate different pyrimidine tracts.

Attempting to define more precisely the structure of the lambda operator, Maniatis and Ptashne have now (page 133) turned to an ingenious exploitation of two restriction endonuclease enzymes which introduce double strand breaks at different sites in the lambda molecule. When lambda DNA is digested with the Hpa enzyme derived from *Haemophilus parainfluenzae*, it is cut in such a way that two fragments are released which contain the operators; a segment of 350 base pairs contains the left operator and a sequence of 2,000 base pairs includes the right operator. Using the second endonuclease, the Hin enzyme of *Haemophilus influenzae*, each of these fragments can be cut into two subfragments. All four subfragments can bind repressor protein, suggesting that each intact operator can be divided into at least two sequences each of which can independently bind repressor *in vitro* in these conditions.

The order of the repressor binding sites within the operator was assigned by taking each of the fragments of length 35–100 base pairs, previously isolated by degrading the repressor-operator complexes formed with different ratios of the two components, and following the effect of the Hin endonuclease. Each fragment was split into two by the Hin enzyme, one subfragment always constituting a length of thirty base pairs, the other corresponding to the remaining length of the particular O_L fragment. What this means is that the primary repressor binding site (that is the fragment of thirty-five base pairs) lies at one end of the operator sequence, the secondary monomer binding sites extending from it in one direction only, comprising about four units of fifteen base pairs each. The action of the Hin enzyme is therefore to separate the primary binding site from whatever secondary sites are attached to it. Similar results are obtained when the right operator fragments are used instead of the left operator—either can be obtained by using mutants of lambda in which one operator lacks affinity for repressor—so that both left and right operators show the same general form of organisation.

By splitting intact lambda DNA with the *Hin* enzyme, Maniatis and Ptashne orientated each operator sequence. They found that the primary binding sequences of thirty base pairs of the left operator can be retrieved in the same fragment as a sequence corresponding to part of the *N* gene; similarly, the corresponding site for the right operator can be reclaimed in a sequence also containing part of the *toF* gene. The primary binding site therefore lies immediately adjacent, or at least very close, to the genes whose expression is prevented by operator-repressor binding; the secondary sites then extend away from the structural genes which are controlled.

Although these results provide a firm basis for some concepts previously held on less sure grounds, they raise several intriguing questions about the precise nature of the lambda operator-repressor interaction. Most notable, of course, is the dramatic difference between the short sequence of the lactose operator and the complex structure in lambda. An important observation, supporting previous speculations, is that the two lambda operators possess different sequences, and as a result have different affinities for the repressor protein, but nevertheless both function to prevent transcription. Also significant is the difference in affinities for repressor of the various sequences included in each operator. Whatever the nature of the DNA sequences which are recognised by the repressor, they can therefore vary in a way which may in future experiments come to throw an important light on the manner of protein-nucleic acid recognition. A puzzling point is the dependence of the secondary sites upon the primary site in the intact lambda DNA molecule; point mutations, apparently located in the primary binding sites, can prevent repression and so allow development of the phage. This means that inactivation of the primary site renders the secondary sites also unable to bind repressor in such a way as to repress transcription.

A final point of speculative interest is the location of the sites on which the restriction enzymes act. The restriction enzymes, of course, are part of the host cell modification and restriction system, which methylates certain sites of DNA native to the cell and also degrades any DNA lacking the appropriate methylations. It is interesting that the sequences recognised by these enzymes should lie so usefully in the control sites of the phage. One possible reason is that restriction and modification activities rely on symmetrical sequences of DNA, as may also the repressor recognition of DNA, providing an obvious resemblance between the two types of sequence. But in teleological terms, it is possible to wonder whether it is only such a coincidence that locates the host modification and restriction sites precisely where they can do most damage to development of the DNA if endonuclease action occurs.

From our Molecular Genetics Correspondent

Defence Mechanisms in Fish

THE capacity of fish to produce antibody on induction with antigen has been known since the early 1900s, and that this production is temperature dependent has been evident since the 1930s. The range of temperature dependence is related to the fish's natural environment, for example, in the warm water carp (*Cyprinus carpio*), antibody can be induced at 20–25° C but not at 12° C, whereas the sablefish (*Anaplopoma fimbria*), from cold waters

in the North Pacific, will produce antibody at 5–8° C. The induction phase of antibody production in fish is prolonged in relation to mammals—18–30 days for cold and temperate species—though some warm water species will produce circulating antibody in less than 9 days. The antibody titres in fish, however, will often equal or exceed the titres obtained in mammals and the circulating antibody can persist for much greater lengths of time—up to one year.

It might be argued that a low temperature which prolongs the induction of antibody will also reduce the virulence of a pathogen, simply by decreasing its metabolic activity. Accordingly, work has been directed to rendering cultured fish immune to various diseases by using the animal's specific immune mechanisms. This work, although still experimental, has met with considerable success though large scale trials on fish farms have generally not been so satisfactory. Nevertheless the fact remains that many fish seem to be severely handicapped and killed by various diseases in a much shorter time than that required for them to produce a measurable immune response, even when they are held in the most favourable conditions yet made available in laboratories. Although some valuable work is being carried out to investigate methods of immunising cultured fish populations (oral vaccination is of necessity the choice because of the large numbers of fish involved), much more ground work is required before applied research can be meaningful; for instance, little is known of the portal by which many important pathogens gain entry into the host fish. It is already known that antibody can be present in localised concentrations according to the site of application of the immunogen, for example, if antigen is administered intravenously the antibody will subsequently be located in the serum, whereas if antigen is fed to the fish in the food, antibody will subsequently be located in the gut mucus. Thus, for protection it would be important that antibody be induced at the site where the pathogen normally enters the host.

Apart from phagocytosis, the non-specific defence mechanisms have not been intensively studied in the lower vertebrates. In this respect the reticuloendothelial system is extensive in the spleen, kidney, heart, liver and gills of many fish species studied. More recent work, however, is providing evidence for the presence of non-specific substances with possible potent protective activity in the tissues and sera of lower vertebrates. The presence of some of these substances seems to be induced, whereas others may be present as normal constituents; for example, the production of an interferon-like substance in fish is elicited by virus and has been shown to confer considerable protection on susceptible cells. Serum titres of lysozyme have been demonstrated to increase (some 100 times) with increase in temperature and immunisation with bacteria, the increase in lysozyme titre being somewhat in advance of antibody production. This finding is contrary to what has been observed in homeotherms. C-reactive protein (CRP) appears in the serum of mammals during injections with microorganisms and has a non-specific precipitating activity. It is now shown by Baldo (see page 145 of this issue of *Nature*) that a substance which seems to have identical activity to human CRP is present in fish serum and will precipitate with extracts prepared from bacteria, fungi and nematodes. Furthermore, it seems likely that this substance is a normal constituent of sera from healthy fish. This could

therefore provide the fish with a potent defence against invading micro-organisms without there being a lag-phase for induction to take place.

An important problem in assessing the results obtained from experiments in fish physiology lies with the technique of husbandry, for the nature and the effect of suboptimal conditions are poorly understood; for instance little is known of the effect of population density, type of diet, handling techniques, nature of water flow and nature of the tank bottom, especially for burrowing species. Husbandry regimes may be stressful and cause a reduction in antibody production on challenge with an antigen, while at the same time increasing stress-induced non-specific substances like interferon and mammalian CRP. Certainly as techniques have improved for maintaining fish in laboratories, many more species have been shown to be immunologically reactive when they were suspected not to be so before, with the notable example of the hagfish, which was until very recently believed to be below the phylogenetic level of adaptive immune capacity.

The prospects for immunological studies in the lower vertebrates are exciting especially with the interest today in the evolutionary and phylogenetic aspects of immunology. Zoologists and medical immunologists are cooperating and the knowledge gained from the evolutionarily simpler systems may well have considerable influence on the understanding of the more complex mammalian counterpart.

A. E. E.

FOETAL ABNORMALITIES

Detection of Defects

from a Correspondent

SINCE many countries have relaxed their abortion laws there was a great deal of interest at the Fourth International Conference on Birth Defects (held under the auspices of the National Foundation March of Dimes in Vienna from September 2-9) in methods for the early prenatal detection of birth defects.

J. W. Littlefield (Massachusetts General Hospital, Boston) and C. Valenti (State University of New York, Brooklyn) emphasised the value of early amniocentesis in suitable pregnancies, especially for the detection of foetal chromosomal anomalies and to a much smaller extent biochemical errors. The apparent safety of early amniocentesis was shown by the results of a questionnaire survey carried out in the United

States; in more than 1,600 amniocenteses only ten errors of diagnosis were reported and the maternal and foetal morbidity attributed to this technique was almost nil. Spontaneous abortions following amniocentesis were less common than would be expected for this stage of pregnancy.

Some means for obtaining samples of foetal skin or blood are needed if many more biochemical errors are to be diagnosed *in utero*. This applies particularly to the common haemoglobinopathies. The use of the fibre optic foetoscope would be of great value in allowing samples to be obtained under direct vision, but J. B. Scrimgeour (University of Edinburgh) made it clear that the difficulties (and hazards) of foetoscopy hardly justify the routine use of this technique. By contrast S. Campbell (Queen Charlotte's Maternity Hospital, London) was very optimistic about the expanding use of ultrasound detection of foetal abnormalities (although the foetus is rarely still *in utero*, making it difficult to get a good picture), believing that it will be possible to diagnose some cases of spina bifida, congenital heart and renal disease as well as to measure foetal urinary output by successive measurements of bladder size. The value of serial measurements of biparietal diameter in detecting low growth potential as an indicator of, for example, chromosomal abnormalities was stressed. Ultrasound is non-invasive and has no known hazards at the intensity and pulse length used. D. J. H. Brock (Western General Hospital, Edinburgh) discussed his empirical but pragmatically crucial discovery that amniotic alpha foeto-protein levels are increased in conceptuses with neural tube defects.

Population screening and subsequent counselling aiming to prevent marriage between carriers of the same genetic disease may prove irresistible to public health authorities seeking a sequel to the successful control of epidemic infectious disease. But the experiences of G. Stamatoiyannopoulos (University of Washington, Seattle) should prove a deterrent to excessive zeal, as even a well planned programme involving the sickle cell trait in Greece resulted in the stigmatisation of families following the collapse of marriage plans and the false belief among carriers that they were diseased and it achieved little or nothing in the way of actually reducing the number of heterozygotes marrying.

Mandatory screening, such as has apparently been imposed by some of the States in the United States on blacks, is to be condemned. By contrast M. M. Kaback (Harbor General Hospital, Torrance, California) described the successful screening programme for detecting carriers of Tay-Sachs disease among Ashkenazi Jews in the United States by

ASTRONOMY

Comet Kohoutek



This photograph of Comet Kohoutek was taken by the Royal Greenwich Observatory, Herstmonceux, at 05.00 h on Tuesday (November 6) using a 6-inch diameter lens at $f/4.5$, exposed for 8 minutes on a Kodak II a-O plate. The comet is clearly distinguished from the surrounding stars by its fuzzy appearance, and in particular by its tail, which extends away from the Sun. The scale of the photograph is indicated by the line which represents the radius of the full Moon. When the photograph was taken the comet was 182 million miles from the Earth.

The speed of the comet relative to the Sun was 22 miles per second, so that, during the 8 minutes' duration of the exposure, the comet moved more than 10,000 miles closer to Earth. Recent forecasts suggest that, at its brightest, the comet will be about as bright as the brightest star, Sirius. It may therefore not be bright enough to see in daylight, but should be easily visible in the twilight sky.

finding reduced levels of heat labile hexosaminidase A in serum and leukocytes. Where both husband and wife were deficient, antenatal diagnosis was carried out (in five pregnancies so far) and one foetus was found to have no heat labile hexosaminidase A activity, and was aborted. The success of the Tay-Sachs programme can be attributed to the education level of American Jews and to the availability of an effective means for antenatal diagnosis and induced abortion when necessary. The general value of genetic counselling was upheld by C. O. Carter (MRC Institute of Child Health, London) provided that it is non-directive and follows the initiative of patients rather than doctors.

J. Edwards (Birmingham Maternity Hospital) stressed the non-eugenic nature of genetic counselling conceding its value in assisting individual families.

Genetic engineering was discussed widely. P. A. Marks (Columbia University) described the use of avian myeloblastic virus reverse transcriptase in the production from natural mRNA of DNA coding for alpha and beta globin chains. The major portion of globin structural genes were synthesised and could in turn be used in heterologous cell free systems or intact oocytes to synthesise the appropriate globins. C. Merrill (National Institute of Mental Health, Bethesda) described possible means of introducing new genetic material into intact cells using the examples of prokaryotic genetic exchange. In a workshop on "Advances of Treatment of Hereditary Metabolic Disease" A. G. Bearn (New York Hospital, Cornell Medical Center) reviewed the use of organ transplantation, particularly the apparently successful use of renal allotransplantation in Fabry's disease, but was quite properly cautious about advocating liver transplants in Wilson's disease treatable by less heroic methods.

Of particular interest was the suggestion by P. E. Polani (Guy's Hospital, London) that mucopolysaccharidosis might be controlled by small skin grafts. H. W. Rudiger (University of Hamburg) described the 'Hunter corrective factor' and discussed how it might be produced from urine for therapeutic purposes. It is curious that earlier pyrogenic samples were most efficient in inducing mucopolysacchariduria.

R. G. Edwards (University of Cambridge) reviewed advances in reproductive biology and their implications and discussed the partial success achieved in the selection of X or Y bearing spermatozoa and *in vitro* fertilisation of human ova. There is no doubt that meiotic and early post-fertilisation studies would greatly assist in explaining non-disjunction and polyploidy. It is astonishing how much interference morulae and blastocysts will tolerate and still (in the mouse) develop into a normal foetus. It had proved possible to disaggregate and mix cell lines for study and to cut embryos in half using one half for study and the other half after implantation develops normally. The rarity with which malformed foetuses resulted from the implantation of animal ova fertilised *in vitro* will no doubt encourage those who would do the same in humans.

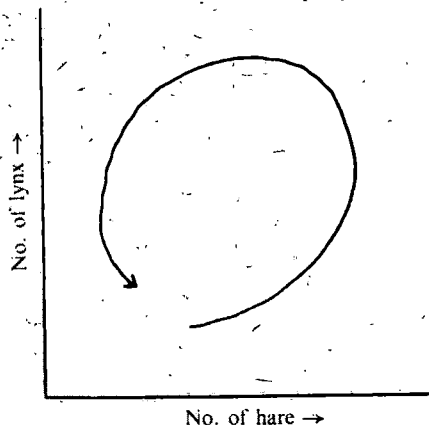
The moral and ethical issues in biomedical research were brilliantly reviewed by A. G. Mutoulsky (University of Washington) who avoided most of the clichés in considering the implications of the present rapid expansion of technology.

POPULATION ECOLOGY

Hare-Eats-Lynx Effect

from our Animal Ecology Correspondent

MOST biologists are familiar with the concept of population cycles and in particular with the well known and often quoted Canadian lynx-snowshoe hare interaction (MacLulich, *Univ. Toronto, Stud. Biol. Ser. No. 43*; 1937, *inter alia*). The provisions of the Lotka-Volterra equations, developed to describe the dynamics of predator-prey interactions, dictate that peaks of predator density must, temporarily, succeed peaks of prey density. When this dynamic arrangement is depicted according to Rosenzweig and MacArthur's graphical predation theory (*Amer. Nat.*, 97, 209; 1963), with the numbers of predator on the ordinate and numbers of prey on the abscissa, the representation of one complete cycle of interaction is a quasi-circular figure progressing in a clockwise direction (see figure).



It comes as a considerable surprise to read the results of Gilpin's subjection of MacLulich's data to Rosenzweig and MacArthur's graphical analysis (*Amer. Nat.*, 107, 727; 1973). He reveals that, for the 30 years 1875-1906 at least, the figure follows an anti-clockwise direction. This presents a severe interpretational problem because hares simply do not eat lynx. Other 10-year interactions, however, had the expected phase relationship. Gilpin and his colleagues (*Theoretical Population Biology*, in the press) have developed a predator-prey model in which growth rates of low density single species, interspecies coupling constants, intraspecific social interactions and intraspecific interference are considered. This model is much more flexible than the Lotka-Volterra one since it assumes that intraspecific factors are important. When the 30-year lynx-hare data in question were examined by this model the regression fit was poor. So poor that the signs of interspecies coupling constants were reversed. The model reinforced the findings of the graphical analysis that the hare was the predator. How, then,

can the anti-clockwise figure be explained?

Gilpin argues that hares could "kill" lynx if, for example, they carried a disease to them. He investigated the possibilities of this by writing an "epidemic" into his model which took effect only when a certain threshold density of hares had been reached. The "disease" was non-fatal to hares but took its toll of lynx. The results of the "epidemic" on the interaction when expressed graphically closely resembled the plot of the interaction during the 30 unexplained years. This explanation seems to be plausible but for the fact that no such disease has been found to occur in reality. Epidemic disease fatal to hares but not to lynx has, however, been identified (Chitty, *J. Anim. Ecol.*, 17, 39; 1948).

The uniqueness of the series of data on the lynx-hare interaction lies in the number of years over which it was collected. Methodically logged by the Moravian Mission in Ungava since early in the last century, the figures for both species are the number of those trapped, skinned and put up for sale. Perhaps Gilpin has hit the nail on the head when he considers that fur trappers themselves are that elusive "disease". During lean years they turn their attention to chores other than trapping and head for the trap lines only when hares are again abundant. If, once at the lines, they turn a disproportionately large amount of their time to lynx trapping (which is infinitely more profitable and therefore reasonable to assume), they would return bags not inconsistent with the data that produce the curious hare-eats-lynx effect.

MacLulich's classic data may constitute the largest series of its kind on record but, as an indicative statement of actual population densities, their validity may be seen by this model to be in doubt. The model may yet be found to be of widespread ecological use, but the test of it will be as good as the test data.

AIR POLLUTION

Ozone and Wild Plants

from our Plant Ecology Correspondent

MOST of the concern surrounding air pollution in western Europe has centred on sulphur dioxide. In North America ozone has long been recognised as an important phytotoxic pollutant produced in the lower atmosphere by photochemical oxidation of certain products of combustion, especially nitrogen dioxide. The production of ozone is therefore particularly prevalent in urban environments where fossil fuels are combusted in large quantities, especially by automobile engines. Nitrogen dioxide formed in this process is split by ultra-

violet light to nitric oxide and atomic oxygen. The latter combines with molecular oxygen to form ozone. In the Los Angeles basin of Southern California daily peaks of ozone concentration of 15 to 38 p.p.h.m. (parts per hundred million) are frequent in summer and autumn. Even the remote areas of North America often have background concentrations of about 2 p.p.h.m.

Although it is known that ozone is phytotoxic, the threshold concentrations at which toxicity becomes apparent are known for relatively few species. Symptoms of external injury include chlorotic and necrotic lesions, but long before these appear a variety of metabolic processes, including photosynthesis, mitochondrial activity and amino acid synthesis, are affected, as well as membrane permeability. The critical exposures which cause such damage have been examined for some crop and tree species, but little is known of the response of natural plant communities.

Treshow and Stewart (*Biol. Conserv.*, 5, 209; 1973) now have data on the threshold levels of ozone resulting in injury symptoms for a variety of wild plant species. The plants were enclosed in portable fumigation chambers in the field within grassland and woodland habitats in Utah and were exposed to ozone concentrations of 15, 25, 30 or 40 p.p.h.m. for 2 h; they were examined immediately after the experiment and again 2 days later. The experiments were thus concerned with short term, acute ozone pollution rather than long term chronic effects.

Of the seventy species examined, several, including *Bromus tectorum* and *Populus tremuloides*, both important or even dominant species in some types of grassland and woodland in the area, showed visible symptoms of injury after just 2 h exposure at 15 p.p.h.m. ozone. Only five species showed no signs of injury after 2 h exposure to 40 p.p.h.m. ozone. This range and order of sensitivity to ozone agrees well with data already published on crop plants.

Ambient ozone concentrations were generally lower than 15 p.p.h.m. In clearings a level of 9 p.p.h.m. was occasionally reached, but beneath the tree canopy in woodland, values were often less than 1 p.p.h.m. This does not necessarily mean that vegetation was unaffected, since damage at a physiological level normally precedes morphological damage and occurs at lower levels than chlorosis and necrosis. It is also possible that reproduction and germination might be impaired by chronic, low level pollution, which would result in long term changes in the composition of the vegetation.

Treshow and Stewart consider it possible that in time sensitive species may be eliminated, leaving unoccupied

niches and bare ground, which would result in a loss of stability in the vegetation. This is an unlikely event since there are several very resistant species in the communities, including some woody perennials (for example, *Acer grandidentatum*). Changes in vegetational composition could, however, have other repercussions such as the reduction of the productivity of an ecosystem.

BURROWING ANIMALS

Airing the Prairie Dog

from our Animal Behaviour Correspondent
PRAIRIE dogs (*Cynomys ludovicianus*) have a problem. These rodents live in long narrow burrows (about 12 cm wide and up to 30 m long) which must somehow be ventilated. Vogel, Ellington and Kilgore (*J. comp. Physiol.*, 85, 1; 1973) have calculated that, at the very least, there must be complete exchange of the air in the burrow with the atmosphere every 10 h and probably more often. They found that neither diffusion of oxygen through the soil or at the burrow entrance nor the direct action of the wind adequately explains how gas is exchanged with the atmosphere to meet the respiratory needs of the animal. How then do the prairie dogs avoid suffocation?

Vogel *et al.* argue that two physical principles may underlie the ventilation. One is Bernoulli's principle in which

flow is related to pressure differences generated by variations in velocity along a streamline. The other is 'viscous sucking', the attraction of stagnant fluid to adjacent rapidly moving fluid. Either mechanism demands that the two entrances to a burrow be dissimilar. Now it has been known for some time that prairie dogs do indeed build two sorts of entrance to their burrows: 'dome craters' (wide and rounded) and 'rim craters' (narrow, steep-walled, with a rim). But the functional significance of these two types was unknown.

Investigations showed that the typical burrow in a prairie dog town has a rim crater at one end and a dome crater at the other. By dropping smoke candles down some burrows, it could also be shown that when even a slight breeze blew, air entered the burrow through the lower mound and left it through the higher one and that the air in the burrow was completely changed in less than 10 min. They then made scale models of prairie dog burrows in which the height and shape of the mounds at each end could be altered, and found that adequate ventilation would result if the mounds at each end of the tunnel were different either in shape or in height. Real mounds are different in both height and shape, which enhances their effectiveness. The authors point out that this ventilation is efficient almost regardless of which direction the wind is coming from and works even when there is very little wind at all.

Positive Control of Enzyme Synthesis

THE appearance of three articles on the control of repression of the tryptophan operon (*Nature new Biol.*, 245, 131, 133 and 137; 1973) leaves no doubt that negative control of enzyme synthesis exists. More recently (see *Nature*, 245, 407; 1973), it was suggested that positive control for biosynthetic schemes must also exist, and indeed that is precisely what Levinthal, Williams, Levinthal and Umbarger put forward in *Nature New Biology* next Wednesday (November 21).

Levinthal *et al.* have isolated a mutant in *Escherichia coli* K12 that renders the cells sensitive to leucine. The system being examined is the biosynthesis of isoleucine, valine and leucine, so it is no surprise that the enzyme threonine deaminase (specified by the *ilvA* gene) is involved (see *Nature new Biol.*, 244, 34; 1973). Moreover, the *leu^s* mutation has been located within the *ilvA* gene, and it has been found to affect the regulatory properties of threonine deaminase with no concomitant alteration in its catalytic activity.

This unique class of *ilvA* mutant (note that *ilvA* encodes the enzyme threonine deaminase, the first enzyme in isoleucine biosynthesis, and is feedback-inhibited

by isoleucine) affords the putative regulatory role of threonine deaminase to be separated from its catalytic function in isoleucine and valine biosynthesis. The regulatory role not only involves the *ilvADE* operon and the genes *ilvB* and *ilvC* but also, predictably, is involved in the control of the amino acyl tRNA synthetases for isoleucine, valine and leucine.

Earlier Hatfield and Burns (*Proc. natn. Acad. Sci. U.S.A.*, 66, 1027; 1970) had proffered a model to explain such regulatory properties inherent in threonine deaminase; they provided genetic and physiological evidence for the role of the enzyme in regulation of the pathway (at the level of synthesis). They suggested, however, that negative control may apply. Next Wednesday's paper by Levinthal *et al.* indeed confirms their idea that the *ilvA* gene product, strategically located, is a key regulatory target in the cell.

The *leu^s* mutant is found to be recessive to the wild type allele. This indicates the absence of function in the *ilvA* mutant and thus allows Levinthal *et al.* to aver that the wild type gene (*ilvA⁺*) produces a positive effector for the control of enzyme synthesis.

GRAVITATION

Radiation and Collapse

from a Correspondent

SYMPOSIUM 64 of the Extraordinary General Assembly of the International Astronomical Union, held in Warsaw on September 5–8 to commemorate the 400th anniversary of Nicholas Copernicus, reflected the growing interest in general relativity among astronomers and astrophysicists. Entitled "Gravitational Radiation and Gravitational Collapse" the programme ranged over most of the areas where it is believed that general relativistic effects are or soon will be susceptible of observation.

Pre-eminent among these areas is the question of the claims of J. Weber (University of Maryland) to have observed gravitational radiation. His colleague C. Misner reviewed the largely unsuccessful attempts of theoreticians to create models of the copious sources of gravitational waves required by Weber's claims. A short report by A. Poveda (University of Mexico) of a new (remarkably low) upper limit to the rate at which the Galaxy is losing mass of 1 solar mass per year, deduced from the orbits of globular clusters, will not make this task any easier. A. Tyson (Bell Laboratories) followed with an account of the current observational situation in which several groups have sought to repeat Weber's experiments with detectors which are claimed to be of equal or better sensitivity than Weber's 1969–70 antennae and have been unsuccessful.

An afternoon session was devoted to a discussion of these results between the parties involved. In particular R. Drever (University of Glasgow), P. Kafka (Max Planck Institute, Munich) and Tyson presented results which indicate that either Weber has not been seeing gravitational waves or that the source has weakened since 1970. On the other hand Weber made renewed claims concerning coincidences both between his own antennae and between his and those of D. Douglas (University of Rochester). The latter, which amount to some fifty-four zero delay coincidences above random in 7 days worth of data, represent an effect at the 2.7 standard deviation level. The fact that Douglas's instrument operates at 710 Hz would indicate that if this effect is real the signals really are broad band, as has long been suspected. It is hoped that the resolution of the puzzle will be brought about by further plans to exchange tapes and subject the raw data to a variety of signal processes, each favoured by one or other experimental groups. Of future plans perhaps the most striking was V. Braginsky's (State University of Moscow) idea of using a massive monocrystal instead of an aluminium bar with a resultant very

high quality factor to look for the sort of signals astronomers expect from nearby galaxies or gravitational bremsstrahlung produced by close encounters of stars—an idea emphasised by Ya. Zeldovich (Institute of Applied Mathematics, Moscow). Some encouraging progress was also reported on the supercooled detectors.

In the light of this it was amusing to hear J. Faulkner (Lick Observatory, California) suggesting that the effects of gravitational radiation might be found on our own doorstep, so to speak, in that mass transfer taking place in very short period binary star systems seems to be controlled in part by the radiation of angular momentum by gravitational waves.

Rather more positive were the sessions on collapse and black holes. R. Giacconi (American Science and Engineering) summarised the wealth of data from optical, radio and most importantly X-ray observation indicating that Cyg X-1 and SMC X-1 may possibly contain black holes. R. Kraft (Lick Observatory) was able considerably to strengthen the evidence by obtaining a lower bound to the distance to Cyg X-1 and hence a lower bound of $6 M_{\odot}$ to the mass of the

unseen secondary. There was, of course, much discussion of accretion models for such X-ray sources and this underlined the importance of numerical work by S. Teukolsky and W. Press (California Institute of Technology) on the stability of rotating black holes and although not everybody will agree with A. Starobinsky (Landau Institute, Moscow) that his ingenious analytical results on super-radiant scattering of waves off black holes, thereby increasing the energies of the waves at the expense of the black hole, guarantees that stability, they clearly represent important advances in black hole theory. The larger issue of "naked singularities" and whether a black hole can shed the respectable clothing of its event horizon to reveal the singularities inside in more extreme situations than those envisaged in the perturbation approach of Press, Teukolsky and Starobinsky were taken up by R. Penrose (University of Oxford) who provided a useful new definition of naked singularities and repeated previous warnings that the mathematical evidence against such objects is largely non-existent.

Among other topics discussed was the report by B. Carr (University of Cam-

Markers of CNS Malformation

SPINA bifida and anencephaly, two closely related malformations of the central nervous system (CNS), are comparatively common congenital disorders in the population of the United Kingdom, with a combined incidence of about 4 in every 1,000 births. Anencephalics die at birth, but after surgery, children with spina bifida live for a number of years with a high degree of physical and mental handicap. The policy of radical surgical intervention, which prolongs the lives of grossly incapacitated children and puts an enormous burden on their families, has recently been called in question.

A little over a year ago Brock and his colleagues (*Lancet*, ii, 197, 1252; 1972) reported that concentrations of α foetoprotein (AFP) were higher in the amniotic fluids of pregnancies leading to anencephaly and spina bifida. Their study was retrospective—that is, made on amniotic fluids obtained for other reasons and where the outcome of the pregnancy was already known—but it raised the hope of early diagnosis of these conditions followed by termination of the pregnancy. These hopes have now been realised in prospective studies (Lorber *et al.*, *Lancet*, i, 1187; 1973; Allan *et al.*, *Lancet*, ii, 522; 1973) and it is becoming an aspect of routine medical care to monitor pregnancies at risk for CNS malformations through AFP levels in the amniotic fluid. The report of Macri *et al.* in *Nature New*

Biology next Wednesday (November 21) adds a new dimension to these studies in that they have demonstrated a CSF-specific protein in the amniotic fluid of foetal Lewis rats with incomplete neural tube closures. Similar proteins are known in human CSF and, if they leak into the amniotic fluid, may provide another parameter to add to AFP in the early diagnosis of CNS malformations.

The real problem, however, in the antenatal diagnosis of spina bifida is identifying the at-risk pregnancy. Ascertainment through the previous birth of an affected child will allow detection of only a small number of cases, since more than 90% of such children will be born to mothers who have no relevant medical history to alert the obstetrician. Monitoring all pregnancies through early amniocentesis and protein analysis is clearly out of the question. A start to the problem has been made by Brock *et al.* (*Lancet*, ii, 923; 1973) who diagnosed an anencephalic pregnancy through AFP levels in the mother's blood. Presumably this foetal protein crossed the placental barrier from the amniotic fluid. The same is likely to occur with spina bifida, because amniotic fluid AFP is every bit as high. But before large-scale monitoring of maternal serum is contemplated it would be as well to have other markers of CNS malformation. The CSF-specific protein described by Macri *et al.* may be just such a protein.

bridge) on primaeval black holes formed very early on in the history of the Universe. It seems that these very small holes will not grow to gargantuan proportions (that is $10^{16} M_{\odot}$) as had been previously suspected by Zeldovich and Novikov. G. Gibbons (University of Cambridge) outlined some possible quantum mechanical effects associated with very small ($\ll 10^{-10}$ cm) holes, first proposed by S. W. Hawking (University of Cambridge) in collaboration with whom both the above pieces of work were carried out. Of special importance is the question of whether they can possess charge.

After this discussion of gravitational collapses it was peculiarly fitting that S. Chandrasekhar (University of Chicago), the man who in a sense started off the subject with the discovery of the upper limit to the mass of a cold degenerate newtonian configuration which bears his name, should have received the highest award of the Polish Academy of Sciences—the Smoluchowski medal—at this conference. It was also characteristic of his breadth of interests that it was for his work on Brownian motion that he received his award.

NUCLEAR PHYSICS

Continuum Shell Model

from our Nuclear Theory Correspondent

UNTIL fairly recently, nuclear structure and nuclear reaction studies developed almost independently, with occasional connections between the two. It was found most convenient to use a harmonic oscillator potential to generate the wave functions for shell model calculations because of its simple and useful analytical properties. These wave functions are indeed good approximations to the real ones, especially for light nuclei. But this potential arises to

an infinite value outside the nucleus, which ensures that the nuclear wave functions soon fall to zero so that the nucleus is prevented from interacting with anything else.

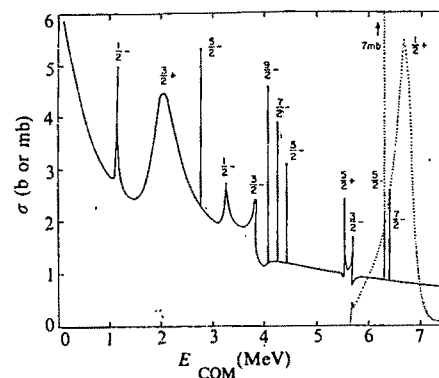
Nuclear reaction studies, on the other hand, have most frequently used one-body potentials like the optical potential to represent the interaction between an incident particle and the nucleus. Such potentials are essentially energy averaged, so that the particular structural characteristics of each nucleus are largely washed out and the potential is almost the same for all nuclei. Thus, paradoxically, nuclear structure theory allowed no reactions, and nuclear reaction theory was almost independent of nuclear structure.

In particular, the shell model calculations, although very sophisticated, could only give the properties of bound states and states that are in reality unstable to particle emission had to be treated as if they did not decay. Reaction calculations, on the other hand, did not include important features of the structure of the interacting nucleus and were then unable to give an adequate account of the increasingly detailed experimental data. This barrier is now being broken down by nuclear structure calculations that include unbound or scattering particles and by nuclear reaction theories that take detailed account of the structure of the interacting nuclei.

A recent example of the former is the continuum shell model calculations of the structure of ^{15}C carried out by Philpott (*Nucl. Phys.*, **A208**, 236; 1973). This is a fully microscopic shell model treatment of the structure of ^{15}C taking account of continuum states as well as bound states and including configuration mixing, finite range and spin-dependent forces and using fully antisymmetrised wave functions. This gives not only the usual shell model states but also a wide range of resonance phenomena, including broad single-particle and narrow many-body resonance in both elastic and inelastic scattering.

To do this the total wave function is expanded as a sum of states, some localised and some describing the separation of a nucleon from the nucleus. If this is inserted into the Schrodinger equation the usual separation procedure gives a set of coupled differential equations for the bound and unbound wave functions, and these can be solved subject to the appropriate boundary conditions.

These equations include matrix elements depending on potentials that have to be specified explicitly before they can be evaluated. These potentials have one-body and two-body components. The one-body component represents the interaction between each active nucleon and the core, and is



tion and discussion. Part of the problem is that the shorter the event the smaller is the chance of detecting it, especially in continental igneous rocks whose sequences are not continuous in time; and even if an event is found to be recorded in more than one lava flow the relevant outcrops are likely to be stratigraphically unrelated. When to these difficulties is added the fact that the errors on potassium-argon ages are usually comparable to the duration of the events being measured, it is easy to see that events will be difficult to resolve. Nor are deep sea sediments likely to provide the final solution, because, as Watkins (*Bull. Geol. Soc. Am.*, **83**, 551; 1972) has pointed out, although sediments frequently form continuous time sequences, the magnetic data from them are not always too consistent and accurate dating methods are even less applicable than to igneous rocks.

The confusion likely to result is well illustrated by the polarity events within the Matuyama reversed epoch from 2.41 to 0.69 million years ago. One of the major normal events is undoubtedly the Olduvai event which was discovered in rocks from the Olduvai Gorge, Tanzania, and later also recognised in lavas from Alaska and the Cocos Islands as well as in deep sea sedimentary cores. The age assigned to the Olduvai normal basalts by Grommé and Hay (*Nature*,

200, 560; 1963) was 1.92 m.y., and so when Chamalaun and McDougall (*Nature*, **210**, 1212; 1966) found normal polarity lavas of ages 2.03 ± 0.05 m.y. (at the normal to reversed boundary) on Réunion island they tentatively correlated them with the Olduvai event while recognising that there was a significant age difference. Later, however, McDougall and Wensink (*Earth planet. Sci. Lett.*, **1**, 232; 1966) discovered another major normal polarity event (the so-called Gilsa event) at 1.6 m.y. in Icelandic lavas; and this was subsequently also recognised in Tenerife, Alaska and Madeira. Moreover, even more recently, Grommé and Hay (*Earth planet. Sci. Lett.*, **10**, 179; 1971) have revised the age of the Olduvai event to 1.72 m.y.

It now seems probable that the Olduvai and Gilsa events are identical, although the identity cannot yet be considered proved. But what is more certain is that the now-named Réunion event first recognised by Chamalaun and McDougall is quite distinct from both the Olduvai and Gilsa events. At the same time, however, the limits of the Réunion event have never been precisely defined; and so to remedy this deficiency, McDougall and Watkins (*Earth planet. Sci. Lett.*, **19**, 443; 1973) have returned to Réunion to study two sequences of olivine basalt lava flows which between them cover the full reversed-normal-

reversed polarity sequence defining the event.

The stratigraphically higher of the two lava sequences was sampled by the two lava sequences was sampled by four reversed flows overlying two normal flows and separated by a flow whose four specimens gave scattered directions of magnetisation. Since this stratigraphically intermediate flow produced fresh specimens petrographically similar to those from the flows immediately above and below, it seems likely that it was extruded during the normal to reverse polarity transition. The stratigraphically lower of the two lava sequences comprised sixteen reversed flows overlain by eleven normal flows, the whole being overlain by a flow of transitional polarity. The two lava sequences may thus even overlap slightly; but, be that as it may, they certainly record the full Réunion event.

From three potassium-argon dated flows in the upper sequence, McDougall and Watkins conclude that the normal to reverse transition defining the end of the Réunion event took less than 30,000 yr and that the absolute age of the transition is 2.02 ± 0.2 m.y. Similarly, from eight dated flows in the lower lava sequence, they estimate the reverse to normal polarity change at the start of the event to have occurred 2.01 ± 0.01 m.y. ago. Clearly, the lack of a significant age difference between the two transitions means that the Réunion event was very short, probably between 10,000 and 50,000 yr long. This shortness probably explains why the event has been recorded so rarely in deep sea cores, and in this, as well as in absolute age, it contrasts strongly with the much longer Olduvai event.

Finally, there has been some suggestion in the past that there may, in fact, be two distinct normal events around 2.0 m.y. ago. Normal polarity lavas in Alaska, for example, have been dated at 1.95 ± 0.10 and 1.96 ± 0.04 m.y., in Argentina at 2.05 ± 0.02 and 2.06 ± 0.03 , and on Cocos Island at 2.09 ± 0.04 . Insofar as all the errors involved here give ranges overlapping, or almost overlapping, the age range of the Réunion event, the corresponding rocks could represent the same event. Similarly the age of the Réunion event as determined by McDougall and Watkins corresponds closely to the age of 1.99 ± 0.06 or 1.97 m.y. for the W anomaly recognised in oceanic ridge magnetic profiles by Emilia and Heinrichs (*Mar. geophys. Res.*, **1**, 436; 1972). On the other hand, anomaly X, identified by Heirtzler *et al.* (*J. geophys. Res.*, **72**, 2603; 1957), has been dated at 2.3 ± 0.1 m.y. As McDougall and Watkins note, their results neither confirm nor refute the idea of a normal event pair; but data already in existence suggest that the polarity-time scale story is still far from complete.

CHEMISTRY

Dimeric Oxygen

from our Chemical Physics Correspondent
SINCE the ground state of an oxygen molecule contains two unpaired electrons, there has for many years been speculation as to whether the dimer, $(O_2)_2$, could form. In 1924 G. N. Lewis suggested, on the basis of measurements on the magnetic susceptibility of the liquid, that some dimerisation does occur, but most of the recent evidence does not support the presence of abnormal forces between two oxygen molecules. Now, from their spectroscopic studies on the cold gas, Long and Ewing (*J. chem. Phys.*, **58**, 4824; 1973) find clear evidence of dimer formation. Nevertheless they note that such dimerisation is of the type to be expected from a typical van der Waals attraction and does not seem to have any exceptional features associated with the unpaired electrons.

Because of its symmetry an isolated oxygen molecule shows no infrared absorption, although at high pressures some very broad features are observed and interpreted in terms of a loss of symmetry during a collision. The collisions are of short duration, so that the uncertainty principle predicts the ob-

served broadness. The new observation of weak, but much narrower, features on top of the band must indicate a longer lived complex. The most prominent features are at 1,553.3 and 1,557.9 cm^{-1} which is the correct position for the excitation of an O-O stretching vibration. The intensity is proportional to the square of the pressure, which indicates a dimer, and although the features are plain at 87 K they disappear above 100 K. Accurate temperature and intensity measurements indicate a molar energy of formation of -2.3 kJ mol^{-1} . The fine structure of eight lines in all has been qualitatively assigned to changes in the relative rotational motions of the molecules with a low hindering potential.

The electronic absorption centred at 17,282 cm^{-1} also has sharp features superimposed on its collision-induced broad line. These confirm the general picture and a fine structure analysis suggests a vibrational interval of 24 cm^{-1} in the ground state for the mode associated with the intermolecular distance coordinate. The value falls to 18 cm^{-1} in the electronically excited level and both are appropriate values for the weak minimum associated with ordinary van der Waals type intermolecular potentials.

Evolution of Insect Wings and Flight

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Disputes during the nineteenth century as to whether insect wings originated from gills or from paranotal lobes ended with almost universal acceptance of the paranotal theory. Sir Vincent Wigglesworth, however, here gives evidence that the thoracic styli were perhaps the precursors of insect wings, and describes a theory of the origin of insect flight.

THE earliest suggestion for the origin of wings in insects was that of Oken¹ who asserted that in the air-breathing Ancylozoa the external branchial lamellae to which the tracheae ran, hardened and were converted into wings. This view was adopted by Gegenbaur²; but a few years later Müller³ noted that the first instar larva of *Kaloterpes* had prominent expansions from the terga of the pro- and mesothorax, and in later instars from the metathorax. He assumed these to be the rudiments of wings; and since, when they first appeared they were devoid of tracheae, he argued from the principle of recapitulation that they could not have been derived from gills and therefore Gegenbaur must be wrong. Many other ideas are commonly attributed to Müller, but that was all he said.

Disputes over these two theories continued throughout the nineteenth century. The decisive paper seems to have been that of Crampton⁴; a highly judicial work in which twenty-one items of evidence are set out in support of the gill theory and twenty-one items of evidence in support of what Crampton named the paranotal theory. He pronounced judgment unequivocally in favour of the paranotal theory. Snodgrass⁵⁻⁷ in all his writings from 1927-1963 took the same view. At present there is almost universal support for this theory.

Packard⁸ had early suggested that the tergal expansions were first used in gliding, perhaps in a leaping insect. Hinton⁹ started further back and stressed the importance of attitude control of legs and body to ensure that a falling insect landed on its feet and could make a quick getaway from predators, notably spiders. Flower¹⁰, assuming that gliding began in a small insect about 1 cm in length, pointed out that even diminutive paranotal lobes would have been important in attitude control. Then hinges to the planes, and muscular control of their inclination, would lead first to control of the direction of gliding and finally to slow flapping flight¹¹⁻¹⁴.

Gill Theory

In working through the extensive literature I came to feel that the case for the gill theory had been too summarily dismissed. I was impressed by Woodworth's thoughtful paper, which took twenty years in the writing. Woodworth points out that gills are soft, permeable, floppy structures, singularly unsuited for conversion into wings operating in dry air. He argues that it is more likely that the wings should have been formed from some structure accessory to the gills and he

develops a case for the mobile gill plates on the abdomen of mayfly larvae being homologous with wings.

As Heymons¹⁶, Börner¹⁷ and others have shown, the gills of *Ephemera* and *Chloëon* are clearly derived from the segmental appendages of the abdomen. The abdominal appendages of Apterygota are represented by the styli. These are not in fact vestigial legs but the exopodites arising from rounded limb bases or coxites, the main appendages or telopodites of which have been lost. In *Ephemera* the appendages are feathered structures; the intrinsic muscles attached to the base of the styli of Apterygota become the muscles which vibrate the gill lamellae. It is in the free-swimming forms such as *Chloëon*, *Baëtis*, and *Ecdyonurus* that they become most wing-like. They migrate laterally and may even become articulated to the dorsum of the abdomen¹⁸.

The vibrating lamellae are not as a rule themselves the gills: they may be only weakly tracheated; they are often stiffened by veins; the leading margin is often rigid and furnished with hairs and spicules; the posterior margin more flexible. The respiratory component takes the form of tracheated filaments, or simply tracheated areas of the abdominal surface. The gill plates serve to drive currents of water over the respiratory surfaces, and may occasionally be used in locomotion.

In the bottom-living larva of *Caenis* the functional gills are limited to the dorsum of segments three to six of the abdomen. As Eastham¹⁹ showed they set up transverse currents across the abdomen. On the second segment gills are wanting, but there is a pair of remarkably wing-like articulated gill-plates (called 'pseudoelytra' by Eastham) which extend backwards to form a gill chamber for the functional gills. In other mayfly larvae similar gill chambers are formed by the backward extension of the wing lobes. Some mayfly larvae have gill filaments arising below the head and thorax²⁰, but wing-like gill-plates are confined to the abdomen. The *Caenis* larva has a little tapering structure, like an unchanged stylus, projecting laterally below the wing lobe; but this is in fact the vestige of the gill belonging to the first abdominal segment and it is articulated to the postero-lateral angle of that segment.

It is surprising that vibratile gill-plates in mayfly larvae should be confined to the abdomen. One would have expected them to be well developed on the thorax, which is the chief locomotor centre with major ganglia and extensive muscles. That is where the gills are always best developed in Crustacea, as in Euphausiidae. The explanation, of course, is that the thorax is already committed to the development of wings. Börner¹⁷ showed that the gill-plates of *Chloëon* arise from the modified limb-bases of the abdomen. In the thorax the limb-base has provided the pleural stiffening of the thoracic box which extends up to the attachment of the wing lobe. There are no gill-plates to be seen.

If there is any real relation between the wing-like gill-plates of the abdomen and the wings of the thorax it must be sought in the non-existent ancestors of the pterygote insects. Fossils of these have not yet been found. The best we can do is to look at the Thysanura, which are the nearest relatives we have of the early pterygotes. *Petrobius maritimus*, for example, is something like a living fossil; it clearly missed the boat, and has been sitting around on the rocks by the seashore since Devonian times. In *Petrobius* and other

machilids, most of the abdominal segments have styli; and they have serially homologous styli of the same character on the meso- and metathorax, the segments on which the wings of Pterygota develop. I suggest that the thoracic styli of machilids were the precursors of insect wings.

Thoracic Styli

The styli of the thorax in *Machilis* arise from the base of the coxa. They have played an important part in the arguments of morphologists. It is because of their survival in *Machilis* that the abdominal styli have been identified as the exopodites of serial appendages of which the limb-base remains but the main limb or telopodite has been lost^{5,21}. Exitae and endites of the proximal limb segment of arthropods, from trilobites to insects, have an extraordinary history. They have furnished most of the remarkable tools of the phylum: mandibles and other mouth parts; gills of trilobites and Crustacea; swimming and grasping appendages; gill-plates of Ephemeroptera; styliiform gills of Neuroptera, Megaloptera and Coleoptera; specialised parts of the external genitalia. Their evolutionary potential is comparable with that of the vertebrate limb.

There seems no reason why a primary apterygote, adapting to aquatic life, should not have developed gills as in the abdomen of Ephemeroptera. Such an insect would have suffered no phylogenetic inhibitions about developing gill-plates from the styli of the meso- and metathorax. In the course of this process, if the changes in the abdomen of mayflies are any guide, the gill-plates would have migrated towards the dorsum and the articulated bases would have become approximated to the terga. It is of interest that certain of the symphylids carry styli on the base of the second and third pairs of legs, and these styli can become incorporated into the cuticular wall of the segment²².

Although the pleuron in insects is believed to be derived from the limb-base, there is no sign of the recapitulation of this process during embryonic development. It is therefore unlikely that we should get evidence in this way of the coxal origin of wings. The most we can hope for is to see the point of origin of the wing rudiment. Tower²³ looked carefully into this question. He showed that in *Periplaneta* the epidermal thickenings, which form the wing lobes, arise on the sides of the thorax at exactly the same sites as in Coleoptera and Lepidoptera; "but (he writes) the wings soon migrate dorsally and posteriorly, and when they become external appear as direct backward projections of the tergum". Tower could thus find no support for the paranotal origin of wings.

The rather weak muscles which actuate the abdominal gill-plates of mayfly larvae, which are derived from the muscles of the styli, retain their attachment to the coxal or subcoxal limb-base. Corresponding muscles would doubtless have been retained by thoracic gill-plates (although the thoracic styli of existing Thysanura, like the corresponding styli in Symphyla, do not in fact retain their muscles). Such a muscular supply would explain why the two most important direct flight muscles in primitive insects (such as grasshoppers) have their origin in the coxa and run all the way through the thorax to be inserted into the basal sclerites of the wing.

Börner¹⁷ established the homology between the gill bases and the thoracic subcoxae, and showed that the tracheae supplying the gills correspond with the tracheae of the thoracic legs. It is interesting that his figure shows the single trachea, which supplies the wing lobe of *Chloëon*, arising from the leg trachea as it runs towards the coxa.

It is likely that thoracic gill-plates would have been supplied by more powerful muscles, and would be larger structures, than the abdominal gills of mayflies. Lubbock²⁴, who accepted the branchial origin of wings, did not consider that the branchiae of *Chloëon* are used in swimming; but he

claimed that in earlier forms, thoracic branchiae might well have been used for locomotion under water. As Lubbock pointed out, the chalcid wasp *Polynema natans*, as he himself discovered, rows its way under water by means of its wings. Although he did not for a moment suggest that this had any direct connection with the origin of flight, it did serve to show that the same wings could be used for locomotion in the air and under water.

It surprises me that the hypothesis here advanced, that the thoracic styli of Apterygota were the precursors of insect wings, which seems a rather obvious suggestion, seems never to have been put forward before.

Origin of Flight

Ten years ago I put forward a 'dispersal theory' of the origin of flight²⁵, without considering the morphological origin of wings. I now attempt to re-state that theory with special reference to the hypothesis that winged insects arose from a secondarily aquatic ancestor.

The existence of a vast aerial plankton of insects and other arthropods extending up into the sky for at least 14,000 foot is well established. Most of these are winged forms; but wingless Thysanura, Collembola, young stages of Hemiptera and Orthoptera, larvae of Coleoptera, Lepidoptera and Diptera and vast numbers of wingless ants have been captured at heights up to 5,000 foot²⁶.

In our postulated aquatic insect, stranded by the drying out of its breeding places, the vibratile gills, even if used for locomotion under water, could not be used directly as propellers in the air; but they would be pre-adapted for development by the insect of the necessary skills, to increase its buoyancy and keep afloat. I picture a small aquatic insect, in the range of 0.5–1.5 cm, as in existing Thysanura, with mobile thoracic gill-plates, which would thus learn to fly while passively air-borne; not, of course, by studying aerodynamics, but by trial and error.

Such an insect would have had no difficulty in adapting to the dry atmosphere. Judging by existing aquatic insects, the integument could well have retained its waterproof properties²⁷. Existing mayfly larvae use their spiracles solely for moulting²⁸; they are not functional in respiration on exposure to the air. In Odonata larvae, however, some of the spiracles do remain functional in aerial respiration. That could well have been so in our aquatic prepterygote. The long slender cerci of Thysanura, as Leston²⁹ has pointed out, could have been an asset for flight stability, as indeed, in conjunction with the long forelegs, they are in existing Ephemeroptera.

The dispersal theory fits in well with our knowledge of the ecology of flying insects. The central idea which I put forward in 1963 was stimulated in part by the work of Kennedy³⁰ on locusts, of Johnson³¹ on aphids and on Rainey's description of dispersal in the desert locust, which is carried by converging winds and lands where the rain falls³². More recently, both Leston²⁹ and Rainey³³ have favoured the idea that insect flight originated in an arid climate. The climate during Devonian times would have provided the conditions needed for this evolution. The combined Lower, Middle and Upper Devonian occupied some 65 m.y. We read about evidence of torrential rains, of extensive swamps, of arid conditions and the formation of aeolian sandstones and wind-driven layers of sand between sedimentary deposits.

Mamajev³⁴ considers that the Devonian insects were associated with the vegetation in the swamp forest along the banks of lakes and that they were probably not true terrestrial forms but followed a semi-aquatic or amphibious mode of life. It would be indeed surprising if, in the course of 50 m.y., the early hexapods had failed to colonise the inland waters. These aquatic animals would presumably feed like mayfly larvae today: by scraping up the algae and diatoms which must have abounded on submerged stones and vegetation. It is likely that they built up gigantic populations, like

mayflies, so that enormous mortality could be tolerated by the stranded migrants. As Rainey³³ has emphasised, arid and semi-arid areas are characterised by vigorous thermal up-currents developing regularly by day over heated ground and rising at speeds of several m s^{-1} . Insects would be caught up also in whirlwinds and dust-devils and carried up into rain clouds.

It is well to recall the parallel theory of Romer³⁵ which describes the evolution of terrestrial locomotion in crossopterygian fishes in their efforts to crawl out of one drying pool during the seasonal droughts of the late Devonian, and hobble over land to another pool with water in it. Walking limbs arose, not in an effort to colonise the land, but in order to survive in water. Likewise in the aquatic ancestors of winged insects: it is suggested that wings arose to make possible a return to water.

I claim, therefore, that the dispersal theory of the origin of insect flight, most of the elements of which have been put forward at one time or another during the past hundred years, offers the least strain to the imagination, because, as Southwood³⁶, Rainey³², Johnson³¹ and others have pointed out, most of the processes involved have been seen in operation around us to the present day.

This article is a summary of a contribution to the Symposium on Insect Flight organised by the Royal Entomological Society of London, September 20–21, 1973:

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Nitrogen Dioxide Concentrations in the Atmosphere

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Nitrogen dioxide and its related compounds react strongly with ozone, usually resulting in the destruction of the ozone, and life seems to be delicately adjusted to the radiation shield which the stratospheric ozone provides. We have found that atmospheric NO₂ occurs in two layers, described here, which have very different properties.

NITROGEN dioxide strongly absorbs visible and near ultra-violet light and for wavelengths between 0.43 μm and 0.45 μm its absorption changes rapidly with wavelength. This permits the measurement of atmospheric NO₂ by measuring its absorption of sunlight, using methods similar to those which have been used for ozone for more than 50 yr (ref. 1). We

have adapted a photon counting spectrophotometer² which was originally designed for ozone measurements for this purpose.

The spectrophotometer measures the intensities at wavelengths $\lambda_1 = 0.4377 \mu\text{m}$, $\lambda_2 = 0.4448 \mu\text{m}$, $\lambda_3 = 0.4500 \mu\text{m}$ with slit widths equivalent to about 0.3 nm. At these wavelengths, and for our slit widths, the solar spectrum is at stationary points and strong differential absorption by NO₂ is achieved. If I_1 is the measured intensity at λ_1 and so on, then after the three intensities have been measured, the function, $F = \log_{10} [I_1/I_2] - 1.46 \log_{10} [I_2/I_3]$, is calculated [$1.46 = (\lambda_2 - \lambda_1)/(\lambda_3 - \lambda_2)$]. This function automatically eliminates all effects for which the absorption at the three wavelengths is linear with wavelength. Ozone absorption is reduced to an extent where it cannot cause interference. Rayleigh scattering, though perhaps not totally removed, is reduced to an unobservable effect. On the other hand, a layer of NO₂ (at STP) 10 μm thick will increase this function by 0.007; which we can measure quite reliably, except when intensities are extremely low. We do not know of anything else with sufficient, non-linear absorp-

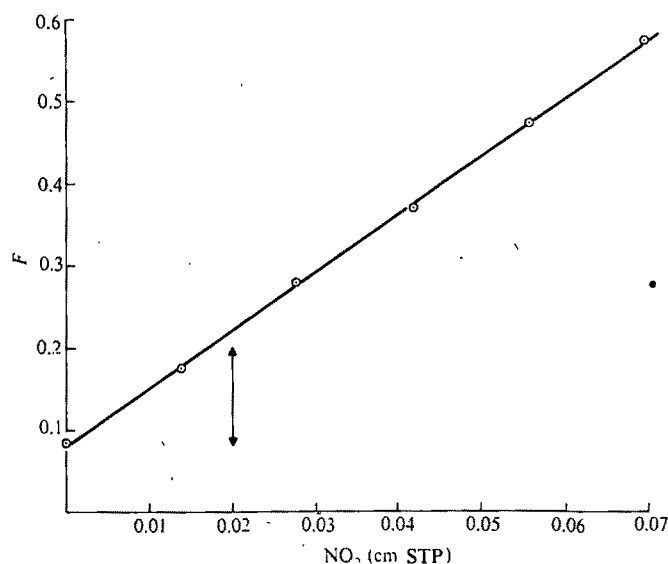


Fig. 1 The growth of absorption by NO_2 , as measured by our spectrograph. The light source was a quartz halogen lamp. To reduce association into N_2O_4 the NO_2 was dispersed in air at room temperature and pressure in a column 30 cm long. F is defined in the text. The vertical line gives the range of optical absorption observed. The slope of the line is 7 cm^{-1} .

tion to interfere. If we displace all our wavelengths by a small amount we can reverse the effect of NO_2 on our function F , though the measurements become less sensitive. The effects we observe are then quantitatively reproduced but with reversed sign as would be expected.

With amounts of NO_2 comparable with those observed in the optical paths attained in the atmosphere we have confirmed the exponential growth of absorption, which has been reported by others³, and also we have measured the value for the effective absorption coefficient, which is consistent with published values (Fig. 1).

Following the analogy with ozone measurements, we have made measurements of the three intensities in direct sunlight and also in the light scattered from the clear zenith blue sky. When these are made for changing solar zenith angles and especially during the periods near sunrise or sunset, when the Sun is low or below the horizon, useful information can usually be obtained about the amount and vertical distribution.

Observations from the ground in Southern Ontario near Picton at 44°N , 77°W , in conditions of clear air with a visibility greater than 30 km and with a cloudless sky, give measurements of which Fig. 2a and b are typical. The differences between sunrise and sunset are persistent and during the first half of 1973 the sky curves have not changed to a detectable extent.

Low Level NO_2

At large solar zenith angles the direct Sun curve is separated from the zenith sky curve because of the presence of NO_2 near the ground, which, when the Sun is low, usually has a considerably higher concentration than exists in the upper air. This may be seen as follows: the light from the direct Sun passes obliquely through the lower layers and their optical effect is enhanced in accordance with the secant of the zenith angle. On the other hand the light from the clear zenith sky is scattered downward by air at rather high levels and it passes through the low level NO_2 vertically, the absorption of which does not become increased by obliquity. We usually assume this low level NO_2 is below 2 km. Deep convection may carry it upward into higher layers but on the clear days when we take our measurements this will not usually be the case. So long as it is below 10 km it will not alter the conclusions we reach in this paper regarding stratospheric NO_2 .

We can also measure the low level NO_2 by climbing through

it and observing the direct Sun while we do so. We have only two measurements of this kind. One made at noon with a solar zenith angle of about 27° (Fig. 7) when we observed very little NO_2 in the lowest two or three km, less than we could measure with certainty, and much less than was measured at sunrise and sunset on the same day. The second measurement was made in the late afternoon with a solar zenith angle of 75° . The quantities found were less than we typically find at sunrise or sunset but were measurable in amount. The actual concentrations found, assumed, in the case of the observations made from the ground, to be distributed through the lowest 2 km, are shown against the appropriate layer in Fig. 4.

The amount is quite variable but it is subject to a strong diurnal variation. There is very little when the Sun is high. There is on the average about 50% more at sunrise than at sunset. We have made observations on the direct Moon; they have low accuracy but suggest that night time amounts of NO_2 are similar to those observed at sunrise.

NO_2 in the Upper Atmosphere

The chief interest centres on the NO_2 in the upper atmosphere and in the stratosphere. We had hoped to obtain this information from the shape of the 'zenith sky' curves, particularly from that part obtained during twilight. This technique is in routine use for deducing ozone vertical distributions and the methods used for inverting the curves have been widely discussed⁴.

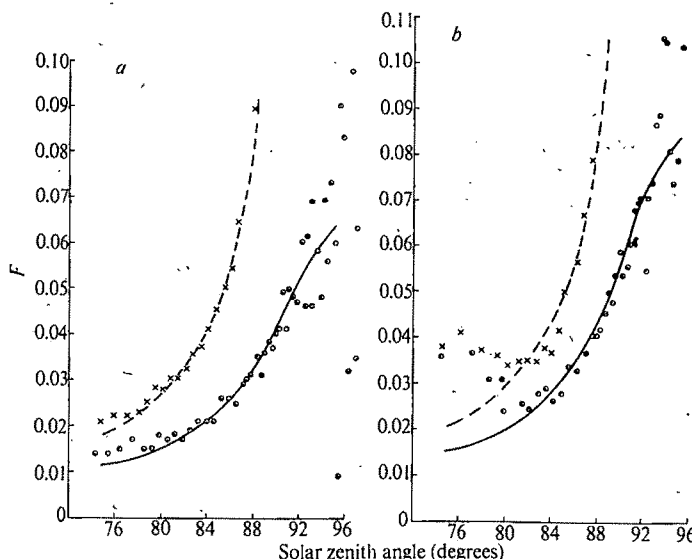


Fig. 2 a, Clear morning observations, July 23, 1973, Picton, Ontario. $\times$, Observed direct Sun; $\circ$, observed zenith sky. ---, Calculated direct Sun; —, calculated zenith sky; both for the sunrise distribution shown in Fig. 4 and using the F_0 as derived in Fig. 6. b, Clear evening observations, July 23, 1973, Picton, Ontario. $\times$, Observed direct Sun; $\circ$, observed zenith sky. ---, Calculated direct Sun; —, calculated zenith sky, both for the sunset distribution shown in Fig. 4 using the F_0 as derived in Fig. 6.

Unfortunately, there is ambiguity about the vertical distributions of the upper atmosphere NO_2 which would produce the observed zenith sky curves. They would be produced either by NO_2 which was almost wholly above 30 km with very little below, or by a suitable NO_2 density at all levels above a few km which changed only slowly with altitude.

The way the ambiguity arises is as follows: it is well known that in the ozone case, the zenith sky curves show an 'Umkehr' and if a well defined layer of NO_2 existed our zenith sky curves would be expected to turn down as the mean scattering level

enters the NO_2 layer and then turn up again when the Sun is below the horizon and the effect of the sunlight passing through the upper part of the layer becomes important. This latter effect which would not arise on a flat Earth is the so called 'second Umkehr'. We observe no vestige of an Umkehr of any kind. This may be because (a) the mean scattering level never enters the NO_2 layer, which, calculation shows, requires that all the NO_2 be above 30 km or (b) there is no layer; that is to say the NO_2 is approximately uniformly distributed through the atmosphere. We do not know of any other way in which the Umkehr can be avoided.

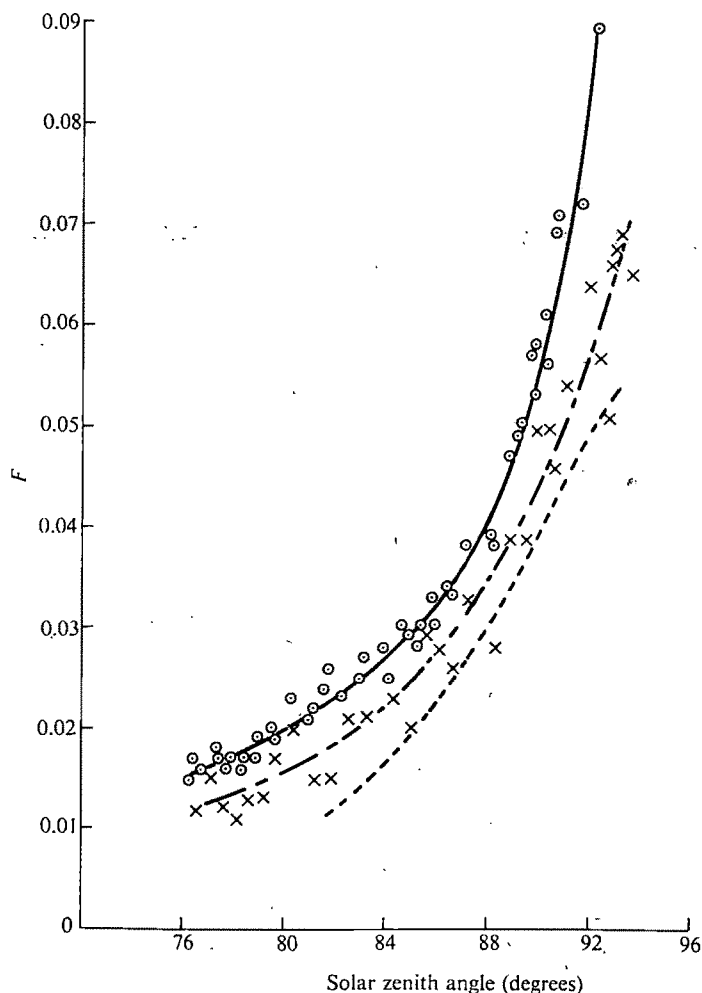


Fig. 3 Observations from an aircraft (12 km), June 13, 1973, Val'd'or, Quebec. $\circ$, Observed direct Sun sunset; $\times$, observed zenith sky sunset; —, mean direct Sun sunset; ---, mean zenith sky sunset; - · -, mean direct Sun sunrise.

Sunrise and Sunset Observations

To resolve this, measurements similar to those described above were made at a height of 12 km at 48°N , 78°W . Because of the height of the observation, the direct Sun could be observed to zenith angles greater than 90° ; this gives the benefit of greatly amplifying the optical path where it is tangential to the Earth, and enables good local concentration measurements to be made at the flight level and below it. The quality and nature of the observations made from the aircraft may be seen in Fig. 3 which shows the observations made at sunset, together with smooth curves drawn through the points. For the morning measurements only direct Sun measurements are available. They are shown in Fig. 3 with data points omitted for clarity.

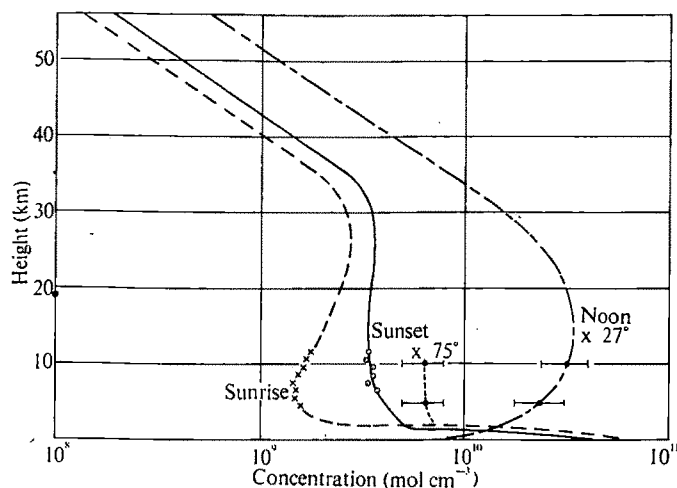


Fig. 4 Vertical distribution of NO_2 in the atmosphere at different times of the day, as measured over Southern Ontario in first half of 1973.

The direct Sun measurements give absolute concentrations between 6 km and 12 km valid for the instant when the Sun is at a zenith angle of 90° . The accuracy and dependability of these values seem high. They are shown as points on Fig. 4. These observations exclude the possibility of all the upper atmosphere NO_2 being above 30 km with very little below.

The deduced upper atmosphere distributions at sunrise and sunset are then as shown in Fig. 4. These distributions are consistent with all the dusk and dawn observations whether from the air or from the ground. The upper air distributions are necessarily strongly smoothed and are very uncertain above 45 km. In Fig. 5 we show the same data plotted as mixing ratio rather than as concentrations. Each layer contributes most to the absorption at the period when the Sun rays are tangential to the Earth; therefore the curves effectively relate to the instant of sunrise or sunset.

The noontime NO_2 is difficult to measure. The presence of a diurnal variation excludes the use of the normal method. This would be to plot the value of F against the secant of the solar zenith angle ($\sec \chi$). The points should lie on a straight line, the slope of which would be the change in F for vertical transmission and would give the total NO_2 overhead. For the whole day the relation between F and $\sec \chi$ is not linear as is seen in Fig. 6. But near sunset (or sunrise) $\sec \chi$ changes

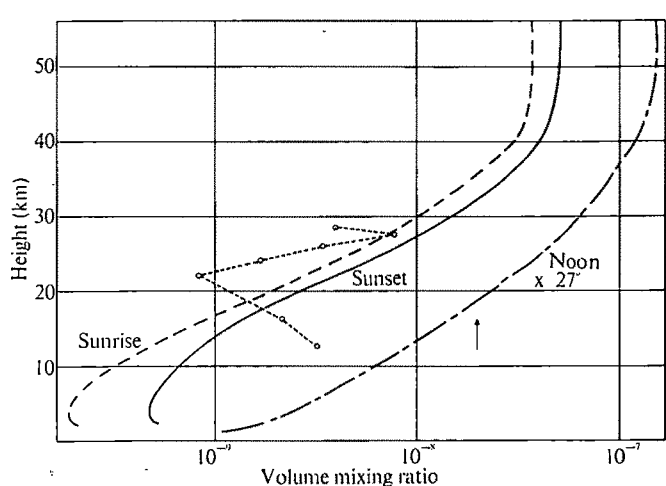


Fig. 5 Vertical distribution of NO_2 in the atmosphere at different times of the day, as measured over Southern Ontario in first half of 1973. For comparison data from Ackerman and Muller⁶ (---) and Harries⁷ (· · ·) are shown on the diagram.

rapidly, and if in this period the NO_2 is not changing too fast then the slope of the line will be the NO_2 present at that time; if extrapolated back to $\sec \chi = 0$, the line will give F_0 , which is the value the function would have if the spectrograph were taken outside the atmosphere. We have normalised this to zero. Thus we consistently obtain a suitable value for the slope and the intersection occurs at a value very much lower than the instrument reads at noon. This indicates that the total NO_2 overhead at noon is very much larger than is overhead at dusk or dawn.

We therefore deduce that the upper air NO_2 has a large diurnal cycle with much larger amounts present when the Sun is high than at dusk or dawn.

Observations at Noon

To investigate this further we made an aircraft flight at local noon with a solar zenith angle of 27° . The aircraft climbed to 11 km and readings were taken of the direct Sun as frequently as possible during the climb and descent. The slope of the observed value of F against height gives the local concentrations. The measured values are shown in Fig. 7. The corresponding NO_2 concentrations are shown in Figs 4 and 5.

If we use these values, together with the total NO_2 , which is obtained from a ground reading at noon and our value of F_0 as discussed above, we have a suggested noontime distribution shown by the appropriate lines in Figs 4 and 5.

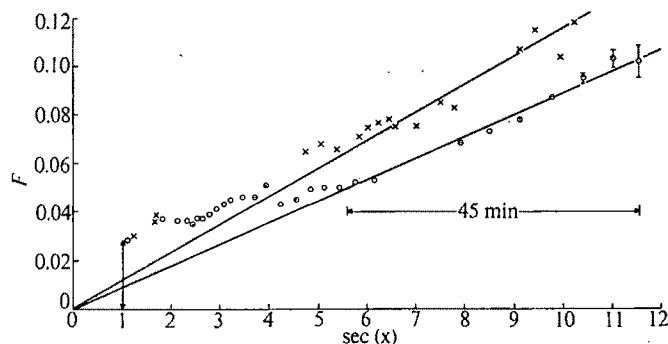


Fig. 6 Observations on the direct Sun, August 3, 1973, Toronto, Ontario. $\times$, Afternoon and evening; $\circ$, morning. The two straight lines are drawn through the points obtained when the Sun is low. Their slope gives the total NO_2 (low level + upper air) at sunset $= 1.65 \times 10^{-3}$ atm cm, and total NO_2 at dawn $= 1.12 \times 10^{-3}$ atm cm. At $\sec \chi = 0$ both extrapolate to F_0 which value is used throughout this work. The total NO_2 at noon was estimated to be 3.5×10^{-3} atm cm.

It is difficult to give absolute limits to the errors possible in these conclusions. The vertical distributions for sunrise and sunset are calculated by finding an NO_2 distribution which, when used in a single scattering model, predicts zenith sky data which agree with observations. The solid lines of Fig. 2a and b are so calculated. If, in any layer between 10 and 40 km, the concentrations are changed from those shown in Fig. 4 by 50% through a depth of one scale height then the fit of the lines to the points becomes unacceptable to the eye. If there were day to day fluctuations of this amount we would notice it in variations of the observations. Similarly if we have wrongly estimated our F_0 by 0.01, which would give an error of 50% in the high noon total of NO_2 , then the curves would be displaced by this amount and it would again be obvious. Errors as large as this therefore seem unlikely.

The diurnal cycle is thus the opposite of that observed in low level NO_2 and is the reverse of that usually hypothesised to occur in the stratosphere. Perhaps the importance of the presence of ozone is underestimated. In the presence of an

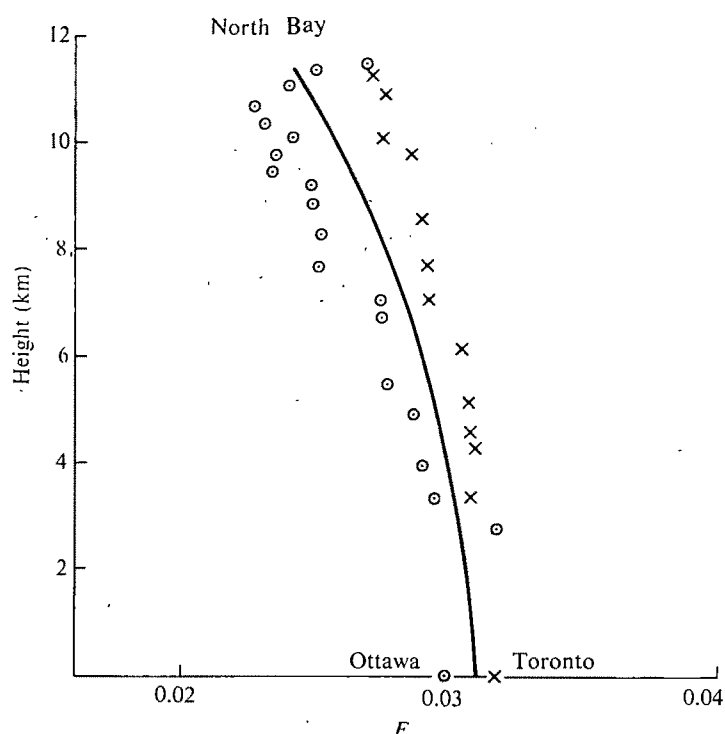


Fig. 7 Direct Sun observations at noon, August 3, 1973. For practical reasons the aircraft flight was from Ottawa climbing to North Bay and descending to Toronto. $\circ$, Observed in ascent; $\times$, observed in descent. Solar zenith angle, 27° .

excess of ozone, as occurs throughout the upper atmosphere, NO_2 reacts with ozone to give NO_3 ($\text{NO}_2 + \text{O}_3 \rightarrow \text{NO}_3 + \text{O}_2$). This reaction, which has been discussed by Johnston⁵, is easy to demonstrate in the laboratory. Ozone and NO_2 will exist together in a glass vessel for days showing the clear blue of NO_3 . We presume that the NO_2 goes to NO_3 by night which is photolysed back into NO_2 by day. NO_3 has optical absorption coefficients (H. Johnston, private communication) which should make its measurement with our apparatus possible. We hope to do so.

Overall Distribution of Atmospheric NO_2

(1) Atmospheric NO_2 occurs in two layers which have very different properties.

(2) Near the ground in relatively unpolluted Canadian air there is a very variable amount of NO_2 of the order of 10^{-3} atm cm. This is present at night. It tends to be larger at dawn than at sunset and is greatly reduced when the Sun is high.

(3) For bright, clear days the total NO_2 overhead in the upper atmosphere does not seem to change very much from day to day, but it has a strong diurnal variation, with a maximum near noon. There is about 0.35×10^{-3} atm cm overhead at sunrise, about 3.0×10^{-3} atm cm when the Sun is high though this measurement is very difficult, and about 0.55×10^{-3} atm cm at sunset.

(4) The concentration of the NO_2 does not change rapidly with height, probably up to 40 km. Expressed as mixing ratio it increases strongly with height probably at least to 40 km. We note that this distribution will result in very heavy downward transport of NO_2 and its associated compounds from the upper stratosphere into the troposphere. Suggested distributions at sunrise, high noon, and sunset are given in Fig. 4.

(5) It seems it would be profitable to look for NO_3 in the atmosphere. We hope to do this.

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the Canadian Department of Transport, provided us with flight facilities during sunrise and sunset. We thank Mr W. T. Tucker for help, and the pilots and the ground staff of the Flight Services Division, Ministry of Transport, for assistance during the flights.

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Structure of the λ Operators

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The two regions of λ DNA to which the λ repressor binds (the operators) are shown to consist of multiple, non-identical repressor binding sites. The arrangement of these sites with respect to the adjacent controlled genes has been determined using a restriction endonuclease that cleaves each operator.

The sites on DNA to which repressors bind are called operators. In the DNA of bacteriophage λ , two operators are recognised by the same protein, the λ phage repressor. These operators are separated by about 3,000 base pairs (bp), and they independently regulate transcription of two separate operons. Repressor bound to O_L blocks leftward transcription of gene N , and rightward transcription of gene tof is blocked by repressor bound to O_R (Fig. 1, and for review see ref. 1).

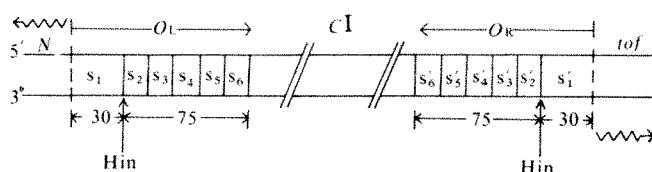


Fig. 1 Schematic representation of the λ operators and adjacent genes. The wavy arrows show the direction of transcription of the repressor-controlled genes N and tof . Two arrows indicate the order of repressor binding from the first sites (s_1 and s_1') to the final sites (s_6 and s_6') in O_L and O_R . The Hin cutting sites in O_L and O_R are indicated along with the number of base pairs within the operators on either side of each Hin cut. The repressor gene is cI .

In this paper we describe certain aspects of the structure of the two λ operators. Our conclusions are summarised in Fig. 1, the essential features of which are as follows. Each operator consists of multiple, non-identical repressor-binding sites. These sites are arrayed in the order shown in the figure: at O_L , repressor first binds to a site (labelled s_1), which is about 30 bp long and is adjacent to N ; subsequent repressor molecules add in linear rightward order to the remaining sites

s_2 – s_6 , each of which is about 15 bp long. At O_R the reverse orientation is found: the site to which repressor first binds (s_1') is at the right terminus, and subsequent repressor molecules bind in linear leftward order. We present here only the essential evidence for these assertions; a more complete description of some of these experiments is found in ref. 2.

The λ operators may be isolated by digesting ^{32}P -labelled λ DNA with DNase in the presence of λ repressor^{3,4}. The protected fragments, bound to repressor, are then trapped on nitrocellulose filters, eluted and examined on polyacrylamide gels. Using the appropriate mutant DNAs it is possible to isolate O_L and O_R separately. We⁴ obtained results of an unanticipated complexity from these nuclease digestion experiments. When the ratio of repressor to operator was increased, six successively larger DNA duplexes were recovered from each operator. The smallest of these was about 35, the largest about 100 bp long, and the intermediate fragments differed in length by about 10 to 15 bp. Analysis of the pyrimidine tracts of these fragments revealed that, at each operator, the site to which repressor first binds is unique (though not necessarily terminal), and that the adjacent sites are then filled sequentially. Within each operator the adjacent sites are not identical repeating sequences and, moreover, the sequences in O_L differ from those in O_R , a finding consistent with the observation that O_L and O_R differ in their affinities for repressor.

Restriction Endonucleases

Our experiments exploit two restriction endonucleases, each of which makes over thirty-five double stranded cuts in λ DNA. One, called Hin , is isolated from *Haemophilus influenzae*, and the other, Hpa , is isolated from *Haemophilus parainfluenzae*. Each is known to be a mixture of more than one restriction enzyme (ref. 5 and Smith, personal communication), but we have found it unnecessary to fractionate these activities. Figure 2 shows the cutting sites of Hpa and Hin in the region of O_L and O_R . The location of these cutting sites was determined in most cases by hybridising the fragments to various deletion and substitution mutants of λ , and in some cases by digesting mutant DNAs and examining the products on polyacrylamide gels². The sizes of the various fragments produced by Hin and/or Hpa , indicated on the figure, were determined as described in ref. 2.

Our restriction endonuclease experiments received their initial impetus from the discovery of Allet⁶ that one of the fragments generated by the action of Hpa on λ DNA is located near the beginning of N , and another includes tof . In collaboration with Allet we found that these fragments, 350 and

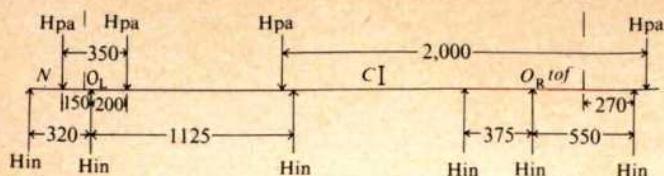


Fig. 2 Schematic representation of a portion of the λ genome showing portions of Hpa and Hin cleavage sites in and around O_L and O_R . The approximate numbers of base pairs between the various cutting sites are indicated. The determination of the various cutting sites is described in ref. 2.

2,000 bp long, bind repressor (unpublished), and further experiments confirmed that they contain intact O_L and O_R respectively². Encouraged by this indication that O_L and O_R can be separated, we sought and found another restriction endonuclease that cuts within each operator. As we shall show, this enzyme (Hin) splits the first repressor binding site from the remaining sites in each operator, and Hin fragments containing either the primary or the remaining operator sites bind repressor.

Operator Fragments produced by Hin and Hpa Cutting of Whole λ DNA

When λ DNA is digested with Hpa, two (and only two) fragments are generated which bind repressor. This is shown by the experiment of Fig. 3a. Hpa-digested, ^{32} P-labelled

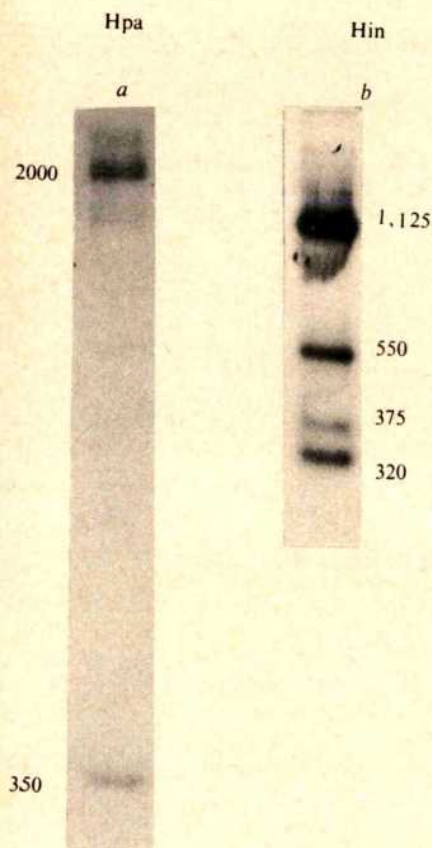


Fig. 3 Operator-containing fragments generated by digestion of whole λ DNA with Hpa and Hin. Hpa and Hin were isolated and used as described in ref. 2. a, 10 μ g ^{32} P-labelled (1.0×10^6 c.p.m. μ g⁻¹) λ DNA was digested with Hpa for 15 h at 37°C in Hpa buffer². Following phenol extraction, a two-fold excess of λ repressor was added to the digested DNA and the mix passed through a nitrocellulose filter. DNA eluted from the filter^{3,4} was examined by electrophoresis through a 4% polyacrylamide Tris-acetate gel¹². b, 25 μ g (5×10^5 c.p.m. μ g⁻¹) ^{32} P-labelled λ DNA was digested with Hin for 15 h at 37°C in Hin buffer²; thereafter the samples were treated as in a. Chain lengths of the duplexes eluted from filters are indicated on the figure.

λ DNA was mixed with λ repressor, passed through a nitrocellulose filter, and the fragments trapped on the filter by repressor were eluted and examined by gel electrophoresis. Two fragments, 350 and 2,000 bp long, were recovered. (The total digest contained over fifty specific fragments (see Fig. 4b of ref. 2).) As indicated in Fig. 2, Hpa 350 contains an intact O_L and Hpa 2,000 an intact O_R .

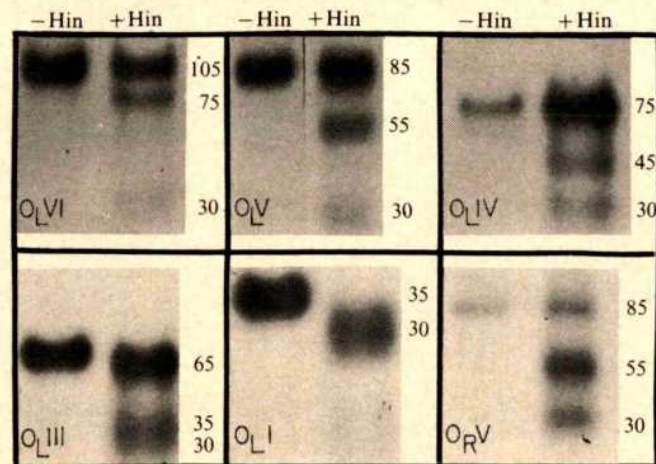


Fig. 4 Hin cutting of isolated operators. Operator fragments (O_{LI} , III, IV, V, VI and O_{RV}) were purified as previously described⁴, digested with Hin for 15 h at 37°C in Hin buffer², and subjected to electrophoresis on a 12% polyacrylamide Tris-Borate-Mg²⁺ gel⁴. Columns labelled '-Hin' show operator fragments incubated under the same conditions but without Hin. Chain lengths are indicated on the figure. In every case except one (O_{LI}) the columns labelled '+Hin' contain some undigested operator, indicating that a limit digest was not achieved.

When this experiment was performed with Hin instead of Hpa, we observed a strikingly different result. In this case four fragments were selectively bound to the filter by λ repressor, indicating that Hin cuts within each operator once, generating two repressor-binding fragments from each operator (Fig. 3b). As shown in Fig. 2, two of these Hin fragments (Hin 320 and Hin 1,125) contain portions of O_L , and the other two (Hin 550 and Hin 375) contain portions of O_R . As predicted from these results, two repressor binding fragments are generated by Hin digestion of either operator-containing Hpa fragment (Fig. 5 of ref. 2). An important conclusion from these experiments is that the secondary repressor binding sites specifically bind repressor even when separated from the primary repressor binding sites in each operator. Thus each operator must contain more than one sequence recognised by repressor. A direct confirmation that Hin cuts each operator is presented below.

Hin Cuts Isolated λ Operators

Five operator fragments were purified from O_L by pancreatic nuclease digestion of the appropriate λ mutant DNA in the presence of varying amounts of repressor as described previously⁴. These duplexes, designated O_{LI} , III, IV, V and VI, are 35, 65, 75, 85 and 105 bp long. Each of these fragments was treated with Hin and the products examined by gel electrophoresis (Fig. 4). In each case two fragments were generated; one was about 30 bp long, and the other varied in length depending on the size of the particular O_L fragment. A schematic representation of the results is presented in Fig. 5. Two important conclusions emerge from this result: (1) Hin cuts once in O_L , near the junction between the first (s_1) and second (s_2) binding sites, and (2) s_1 is terminal, and the remaining sites are filled in linear order.

This experiment has also been performed using the 85 bp operator fragment isolated from O_R (O_{RV}). In this case the

same result was observed as with the corresponding $O_L V$ (Fig. 4). From experiments described below we deduce that the 30 bp fragment split from $O_R V$ by *Hin* is s_1 . We conclude therefore that as in O_L , the first repressor binding site in O_R (s_1) is terminal, the sites are filled in linear order, and *Hin* cuts between s_1 and s_2 .

Orientating the Operators

We have argued that one of the many *Hin* cutting sites in λ DNA is within O_L between s_1 and s_2 , and another is within O_R between s_1' and s_2' . This conclusion predicts that of the two O_L -containing *Hin* fragments generated from whole λ DNA, one should contain s_1 , the other s_2-s_6 . Similarly, the two O_R -containing fragments should contain, separately, s_1' and $s_2'-s_6'$. The experiment of Fig. 6 verifies this prediction and, moreover, reveals the important new fact that each operator is orientated such that s_1 and s_1' are proximal to *N* and *toF* respectively. To perform this experiment, the four operator-containing *Hin* fragments, labelled with ^{32}P , were isolated from whole λ DNA as described for the experiment of Fig. 3, digested with pancreatic DNase in the presence of excess repressor, and recovered from nitrocellulose filters. Figure 6 shows that the two *Hin* fragments known to contain *N* and *toF* sequences (*Hin* 320 and *Hin* 550, respectively, see Fig. 2) yielded duplexes 30 bp long, the known sizes of s_1 and s_1' . Larger pieces were protected from the other two *Hin* fragments: the fragment containing the right part of O_L (*Hin* 1,125) and that containing the left part of O_R (*Hin* 375) yielded, respectively, duplexes 75 and 55 bp long which we identify as s_2-s_6 and $s_2'-s_6'$. (The fact that s_6 was not protected in this particular experiment is consistent with our observation that, compared with O_L , more repressor is required to protect the largest fragment of O_R (ref. 4).)

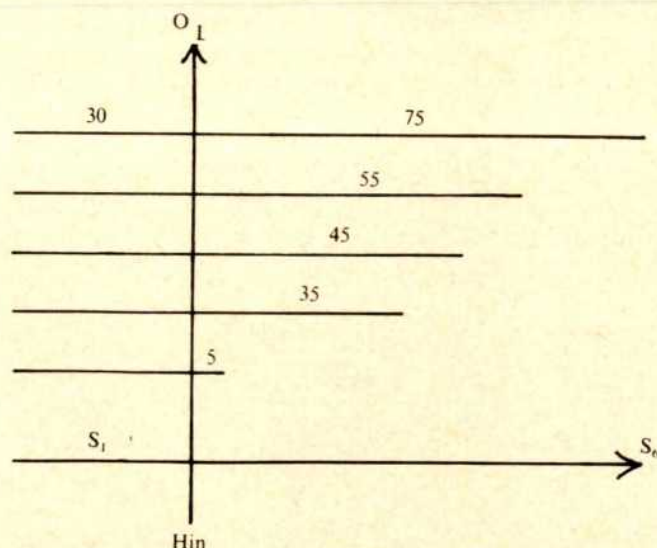


Fig. 5 Schematic representation of the effect of *Hin* on isolated O_L fragments. The vertical arrow labelled *Hin* shows the position of the cutting site within the various operator fragments. The horizontal arrow shows the order of repressor binding sites s_1 to s_6 .

The results of the experiment of Fig. 6, taken in conjunction with the fact that each operator is filled with repressor in linear order, orientates each operator as shown in Fig. 1. s_1 and s_1' are proximal to *N* and *toF* respectively. O_L binds repressor beginning at its left extremity and subsequent repressor molecules are added in a rightward direction, whereas the opposite is true at O_R .

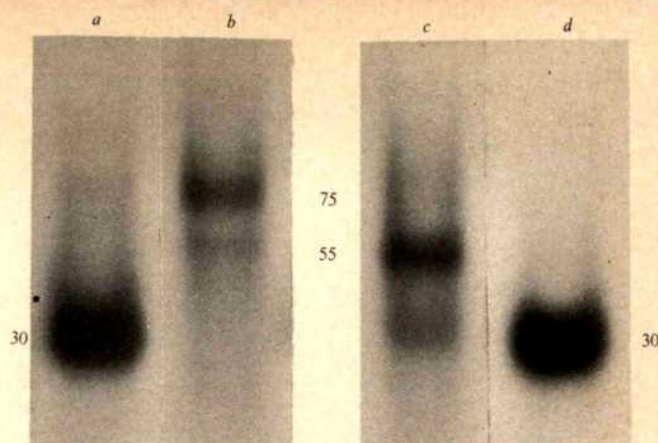


Fig. 6 Operator fragments contained in four *Hin* fragments. The four operator-containing *Hin* fragments were isolated as in Fig. 3b and eluted from the gel. Repressor was added to ten-fold molar excess and the samples digested with DNase^{3,4}. The protected fragments were examined on 12% TBM polyacrylamide gels⁴. Sizes of the protected fragments are indicated on the figure. a, *Hin* 320; b, *Hin* 1,125; c, *Hin* 375; d, *Hin* 550.

Further Results and Discussions

Several additional findings, evidence for which may be found in ref. 2, are as follows: (1) The two *Hin* fragments identified as containing s_1 and s_1' (*Hin* 320 and *Hin* 550) bind repressor more tightly than do the two *Hin* fragments containing s_2-s_6 and $s_2'-s_6'$ (*Hin* 1,125 and *Hin* 375). The order of affinities is *Hin* 320 > *Hin* 550 > *Hin* 1,125 > *Hin* 375. We estimate that, for half-maximal binding, s_2-s_6 requires about three- to five-fold more repressor than does s_1 , and $s_2'-s_6'$ requires about ten- to fifteen-fold more repressor than does s_1' as measured using the various operator-containing *Hin* fragments. (2) An operator constitutive mutation has been located in s_1 . (The repressor affinity of *Hin* 320, but not that of the remaining three operator-containing *Hin* fragments, is reduced (about three- to five-fold) when *Hin* fragments are generated from DNA bearing this mutation.) (3) The distance between the left extremity of s_1 and *N* is less than 20 bp.

The experiments reported here, taken in conjunction with our earlier work², show that each λ operator contains multiple repressor recognition sites. In all, there are at least four and may be as many as twelve different sites specifically recognised by one protein, the λ phage repressor. Although the two λ operators differ in their sequences and affinities for repressor⁴, the arrangement of binding sites with respect to the adjacent controlled genes is the same in the two cases. In both cases the strongest affinity site is adjacent to the controlled gene, and repressor fills the operator linearly in the direction opposite to that of transcription of the structural gene. At least one sequence is common to both operators, namely, the *Hin* cutting site located between the first and second binding sites in each operator.

The λ operators are more complex than the *lac* operator, which consists of a single sequence about 25 bp long⁷. It may be relevant to note that the only molecular species of *lac* repressor known to bind DNA is a stable tetramer of identical subunits of molecular weight 40,000 (refs 8, 9). The λ repressor, in contrast, has the property that its subunit (molecular weight 30,000) is in concentration-dependent equilibrium with dimers and tetramers^{10,11}, and we deduce from the different sizes of the binding sites on λ DNA that more than one form of the λ repressor binds to DNA. Whatever the significance of these observations may be, one principle of DNA-protein interaction that emerges from the study of the λ case is that the presence of multiple, non-identical binding sites enables a small protein to cover a relatively long and unique stretch of native⁴ DNA.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Deuterium Formation Hypothesis for the Diffuse Gamma-ray Excess at 1 MeV

MANY measurements of the diffuse X-ray and γ -ray background¹⁻⁴ indicate that it consists of an inverse power law spectrum with index ~ 2.0 . Spectral features or excesses are reported in the vicinity of ~ 40 keV and ~ 1 MeV. When plotted on linear-linear paper the 1 MeV excess is seen to consist of a pronounced peak in the 0.5 to 2.0 MeV region with a feeble tail extending on to higher energy (Fig. 1). In this paper a simple explanation is presented for the 1 MeV peak in light of new experimental and theoretical advances made in the past year. No explanation is presented for the higher energy excess and it is presumed to come from other mechanisms. I hypothesise that the peak arises from the astrophysical production of deuterium by the two body recombination process ($p+n \rightarrow D+2.2$ MeV γ ray) in an environment transparent to the emitted γ rays. The hypothesis is shown to lead unambiguously to two remarkable numerical results: a calculation of the terrestrial $n(D)/n(H)$ ratio; and a prediction of QSO cutoffs at $z \sim 3$.

The most recent measurement of the γ -ray background made on Apollo 15 has confirmed the 1 MeV feature⁴. Although the large uncertainties associated with this spectrum ($\sim 30\%$) may seriously effect the shape and magnitude of any extracted excess curve, it nevertheless seems reasonable to accept the data at face value and investigate the consequences, bearing in mind that future, more precise data may change the arguments considerably. In Fig. 1 the difference between the Apollo 15 spectrum and an $E^{-2.0}$ extrapolation of the low energy power law portion of the Apollo 15 spectrum is plotted. (The discussion to follow is substantially unaltered by changes in the power of the extrapolation $\lesssim 10\%$.) The Apollo 15 spectrum has been used because it is most recent and spans both the power law and 1 MeV excess regions of the spectrum. Several origins of the feature have already been suggested. These are summarised and discussed in a recent paper by Stecker³. At present none of these has yet been widely accepted. Here I argue generally in support of the position of Clayton and Silk⁵ who suggest that the origin of the feature is in γ -ray lines emitted by heavy radioactive nuclei after their

synthesis in supernova explosions throughout the Universe. But it is suggested in light of recent discoveries that Clayton and Silk⁵ (CS) have not discussed what may be the most important γ -ray line emitted in astrophysical nucleosynthesis, namely the 2.2 MeV deuterium recombination line. The large potential enhancement in γ -ray line signal from this mechanism significantly strengthens the argument for a line origin of the feature.

The unambiguous astronomical detection of deuterium^{6,7} has now removed all doubt concerning its existence on a galactic scale. Some doubt exists concerning its relative abundance, but it is reasonable to assume that the $n(D)/n(H)$ ratio approximates the terrestrial value of $1-2 \times 10^{-4}$ on a galactic scale. In view of this large abundance, Hoyle and Fowler⁸ and Colgate⁹ have argued that the D may be made astrophysically under non-thermodynamic conditions rather

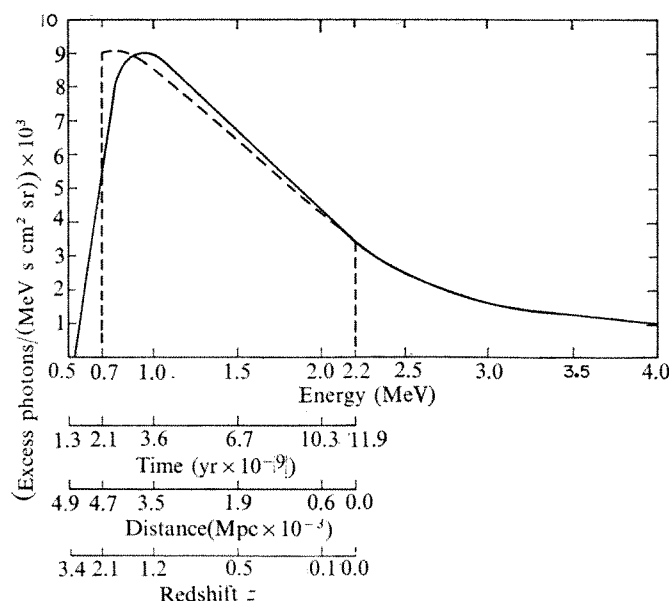


Fig. 1 Plot of the 1 MeV diffuse γ -ray excess above an $E^{-2.0}$ power law extrapolation of the lower energy spectrum. Also shown (---) is a theoretical spectrum based on the deuterium formation hypothesis and cosmological assumption discussed in the text. The energy axis is also labelled in time and distance for the cosmological model used.

than cosmologically. Specifically Hoyle and Fowler suggest that α particles accelerated in a supernova shock wave can produce D and neutrons in the outer envelope by a spallation reaction and the neutrons may subsequently recombine with the ambient hydrogen also to make D. In view of the present rudimentary understanding of the details of supernova explosions, it is difficult to decide whether the direct production of D is more important than the indirect recombination process. Hoyle and Fowler⁸ conclude that the recombination process can be an order of magnitude more efficient if the H gas density is high enough for most of the neutrons to be captured.

Strong evidence in support of the contention that recombination can be an important astrophysical process in an environment which is transparent to 2.2 MeV γ rays was obtained by Chupp *et al.*¹⁰. Observation of two intense solar flares with a satellite borne detector revealed that the dominant feature in the γ -ray spectrum was the 2.2 MeV deuterium recombination line. Ramaty and Lingenfelter¹¹ have shown that the propagation of ~ 10 MeV neutrons in an H atmosphere is determined by elastic and inelastic np scattering with D formation occurring at a range of about 1.6 g cm^{-2} . Since the stopping range of a 2.2 MeV photon is about 25 g cm^{-2} these workers conclude that the solar flare γ rays will escape unattenuated. Although I am not arguing for a solar flare origin of the 1 MeV excess, it is important to see that it is clearly possible to construct astrophysical models which will be compatible with the D hypothesis.

On the basis of a simple abundance argument, $(n(^{56}\text{Fe})/n(\text{H})) = 3.1 \times 10^{-5}$ and the assumption that the ^{56}Fe in the Universe was produced by radioactive decay from supernova produced ^{56}Ni and ^{56}Co , CS concluded that the dominant lines in the 1 MeV excess should be from this process. Their flux estimate indicated that it might be possible to account for most of the excess with these lines. Assuming that recombination is the important D production mechanism on a cosmic scale and noting that the $n(\text{D})/n(\text{H})$ ratio may be an order of magnitude greater, I conclude that D recombination can more easily account for the excess. The subsequent discussion does not depend on a supernova origin of D but only on the pre-eminence of astrophysical D production by recombination and the transparency of the source to 2.2 MeV γ rays. But D formation may take place in the outer envelope of supernova from which the probability of γ -ray detection could be high relative to γ -ray detection of heavy element nucleosynthesis at the core which must await the expansion of the remnant before becoming detectable. Once out of the source, absorption in the interstellar and intergalactic medium is expected to be negligible.

The exact shape of the expected D feature depends on the cosmological model one assumes and also on assumptions concerning the time dependence $f(t)$ of the galactic synthesis rate of D. Clayton and Silk have derived expressions for the shape of the spectral feature anticipated from a single γ -ray line. Clearly one expects an edge at the rest energy of 2.2 MeV and a continuous distribution towards redshifted energies from D synthesised at earlier times in distant galaxies. Eventually at lower energies the distribution will disappear as one looks at the epoch prior to the beginning of astrophysical nucleosynthesis assumed to start at time t_* in all the galaxies.

To show that the observed feature is consistent with reasonable cosmological assumptions a computer constructed plot of the expected shape is given in Fig. 1 for an Einstein-de Sitter universe, $q_0 = 0.5$, $\rho_0 = 5 \times 10^{-30} \text{ g cm}^{-3}$ for which $\gamma = 1.5$. Employing the current value of $55 \text{ km s}^{-1} \text{ Mpc}^{-1}$ for the Hubble constant yields a universe of age $t_0 = 11.9 \times 10^9 \text{ yr}$. The data indicate a rate of nucleosynthesis peaked in the past for which an exponential form $f(t) = f_0 \exp[-\lambda t]$ has been assumed. Following CS, equation (8), a theoretical flux curve of the form

$$F \propto \exp(-\lambda t_0(E/2.2)^{\gamma})(E/2.2)^{\gamma-1} \text{ cm}^{-2} \text{ s}^{-1} \text{ sr}^{-1} \text{ MeV}^{-1}$$

amplitude normalised to fit the data at 2.2 MeV has been used.

At this point it is important to point out that t_* , λ , and f_0 are now determined by the data. The low energy edge at E_* determines $t_* \sim 2.1 \times 10^9 \text{ yr}$ through the expression $t_* = t_0(E_*/2.2)^{\gamma}$; the shape of the 1 MeV feature determines $\lambda^{-1} \sim 6.5 \times 10^9 \text{ yr}$; and its amplitude determines f_0 . The quantity f_0 can most easily be determined from a cosmological correspondence principle—for small distances and redshifts the results of relativistic calculations in curved spaces must go over to the results of non-relativistic calculations in Euclidean spaces. So the incremental flux ΔF in the energy interval E to $E + \Delta E$ and the time interval t to $t + \Delta t$ arises from galaxies at distances r to $r + \Delta r$ and is given non-relativistically for small r by

$$\Delta F = (1/4)n_g f_0 \exp(-\lambda t) \Delta r \text{ cm}^{-2} \text{ s}^{-1}$$

where n_g is the average density of galaxies taken to be $1.0 \times 10^{-75} \text{ cm}^{-3}$. The factor $1/4$ arises $(1/2)$ from the fact that γ rays emitted on the far side of a thick synthesising object like a supernova have no chance of reaching us and $(1/2)$ from the angular distribution of galaxies with respect to a flat 1-cm^2 detector. Using the value of λ determined from the shape of the excess and evaluating ΔF for an interval Δr near $r=0$ yields $f_0 \sim 1.2 \times 10^{47} \text{ s}^{-1}$. In the above estimate I have neglected: (1) all other possible contributions to the 1 MeV excess (such as the ^{56}Ni and ^{56}Co γ -ray lines); (2) the possibility that nucleosynthesis did not begin at the same time t_* in all galaxies; (3) any Compton scattering of the γ rays before detection; and (4) the large energy resolution ($\sim 10\%$) of the detectors employed on Apollo 15. The sharp edge predicted by the D hypothesis at 2.2 MeV is only hinted at in the data, presumably because of instrumental smearing and background effects.

If the above discussion is taken seriously and absorption of the γ rays in the source is neglected the $n(\text{D})/n(\text{H})$ ratio can be estimated in the Galaxy for D produced by recombination. The total number of D nuclei, $N(\text{D})$, is given by

$$N(\text{D}) = \int_{t_*}^{t_0} f_0 \exp(-\lambda t) dt = 1.3 \times 10^{64}$$

Taking the Galactic mass to be $1.1 \times 10^{11} M_{\odot}$ containing 70% H by mass yields $N(\text{H}) = 9.2 \times 10^{67}$. Thus a D/H ratio of $\sim 1.5 \times 10^{-4}$ is obtained which is in agreement with the terrestrial value. Moreover this result is relatively insensitive to cosmological models which basically serve to fix the time axis of Fig. 1 and the specific form of $f(t)$, depending primarily on the area under the curve in Fig. 1. But in the light of the many uncertainties in the above estimate the exact agreement with the terrestrial value must be fortuitous, although it nevertheless indicates that the calculation gives an order of magnitude estimate which is correct. I take this remarkable result to be significant evidence for the correctness of the deuterium hypothesis and hope that it will stimulate the search for the astrophysical origin of D. In particular, models of supernova which allow for large scale D production by recombination and the detection of the 2.2 MeV γ rays should be pursued.

Additional support for the D hypothesis comes from the observation of quasar redshifts $z(z \equiv 2.2/E - 1)$. If QSOs are indeed young galaxies and it is assumed that their emission is not occurring before the beginning of D nucleosynthesis at time t_* then Fig. 1 predicts the large z redshift behaviour to be expected. It is apparent that the number of quasars detected at $z \sim 2$ should be falling off rapidly with the distribution disappearing at $z \sim 3$. This agrees with the experimental evidence.

Finally, experimental support for the deuterium hypothesis could come with the detection of a strong 2.2 MeV line from a reasonably local supernova explosion and/or the detection of a 2.2 MeV edge in the diffuse background. For these measurements the application of a high resolution γ -ray telescope is indicated. Detection of large amounts of D in

the vicinity of a supernova remnant by other means would also be supporting evidence.

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Average Trace Element Composition of Low Level Marine Atmospheric Particulates

GROWING concern has been expressed^{1,2} over the introduction of pollutant trace metals to the oceans through the atmospheric transport of particulates from the continents. Few data exist on the elemental composition of such particulates, and those available are usually from restricted regions³⁻⁵. We have carried out a sampling programme^{6,7} in which particulates have been collected from seawater and from the lower atmosphere (~15 m above the sea surface) over large tracks of the world ocean. The collection details have been described elsewhere⁶ and the distribution of Pb in Atlantic particulates has been reported⁷. Here we present data on the average trace metal composition of aeolian particulates from the lower atmosphere of various major wind systems over the World Ocean.

Particulates were sampled from the following wind systems (number of samples in parentheses): North Atlantic Westerlies (4); Atlantic Westerlies/North East Trades boundary region (3); Atlantic North East Trades (7); Atlantic ITCZ (3); Atlantic South East Trades (5); variable winds, South African Coast (7); North-east Monsoon, northern Indian Ocean (3); variable winds, southern Indian Ocean (3); South-west Monsoon, South China Sea (9); northerly wind, East China Sea (1); variable winds, Japanese coast (6). The average trace metal composition of each of these dusts is given in Table 1.

The distribution of some trace elements in low level marine aeolian dusts can vary geographically⁷. This is particularly true of those elements which have a significant man-induced (anthropogenic) component because the relative proportion of this component will decrease with distance from a specific source of pollution. As a result, concentration ranges in the dusts can be relatively large. But in particulates which are not obviously associated with known sources of pollution it is difficult to distinguish between a natural and an anthropogenic origin of trace elements unless there are data on the average distribution of such elements in aeolian particulates from the

low level marine atmosphere. The data given in Table 1 will help to provide such an average.

To identify those trace elements which potentially have a significant anthropogenic contribution Goldberg² has employed an 'enrichment factor', based on the ratio of an element to iron in atmospheric particulates, divided by the ratio of the same elements in average crustal material. Similar calculations have been made for the elements in the particulates from the low level marine atmosphere. Since the ultimate source of natural trace elements in atmospheric particulates is crustal material, from which they are released by the action of geological processes, the enrichment factors should be around unity if natural sources predominate. But these trace elements can undergo considerable fractionation during processes such as weathering and degassing, and the enrichment factors can only be regarded as indicating to a first approximation those elements which potentially have a significant contribution from an anthropogenic source. From the results which are given in Table 1 it can be seen that for the elements Mn, Ni, Co, Ga, Cr, V, Ba and Sr the enrichment factors are reasonably close to unity; in other words, these elements are not significantly enriched in average low level marine aeolian particulates, and in fact Co and Sr are depleted, relative to average crustal material. In contrast, the elements Sn, Pb and Zn are enriched in the aeolian particulates, relative to average crustal material, by one order of magnitude even when geographical variations are smoothed out by taking a 'world-wide' average. These factors have been used to identify those elements which are contaminating the atmosphere², and it may be concluded that Sn, Pb and Zn are being released preferentially into the marine atmosphere (from sources which probably include the activities of man) and are concentrating, relative to average crustal material, in low level aeolian particulates.

Table 1 Average Trace Element Composition of Low Level Marine Atmospheric Particulates

Element	Concentration	Enrichment factor *
Fe	5.2 (2.2-9.9)	—
Sr	101 (17-203)	0.35
Co	9 (3-36)	0.45
Cr	85 (21-850)	1.2
V	145 (37-530)	1.4
Ba	487 (57-1,100)	1.4
Mn	1,312 (310-3,720)	1.5
Ni	91 (10-720)	1.5
Ga	21 (5-41)	1.6
Cu	157 (23-490)	3.4
Zn	683 (136-3,100)	13
Sn	30 (1-120)	19
Pb	465 (29-2,750)	49

* See text.

Concentrations are in p.p.m., with the exception of Fe which is given in wt %; the figures in parentheses indicate the ranges found.

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New Radiolarian Palaeoclimatic Index in the Plio-Pleistocene of the Southern Ocean

PLIOCENE-PLEISTOCENE palaeoclimatic investigations in the Southern Ocean have been carried out using five groups of microfossils: foraminifera^{1,2}, calcareous nannofossils³, Radiolaria⁴⁻⁹, diatoms¹⁰, and silicoflagellates¹¹. Radiolarian methods are particularly valuable in higher latitudes where carbonate sediments are susceptible to dissolution even in relatively shallow waters^{12,13}. Established radiolarian techniques are based on oscillations of cold-water (Antarctic) relative to warmer-water radiolarian assemblages, established by determining their distribution in Recent sediments relative to the Antarctic Convergence (Polar Front)⁴. The cold-water assemblage used in these palaeotemperature determinations consists of eight species, whereas the warm-water assemblage consists of nine species^{4,9}. Of the several dozen species known in Southern Ocean Quaternary sediments, these seventeen species represent more than 75% of the individuals⁴.

Here I describe a new radiolarian palaeoclimatic method, based on frequency oscillations of *Antarctissa strelkovi* Petrushevskaya, which has been applied to Antarctic and Subantarctic deep sea cores. This species comprises a significant portion of the radiolarian assemblage throughout the Pliocene-Pleistocene in Antarctic-Subantarctic cores.

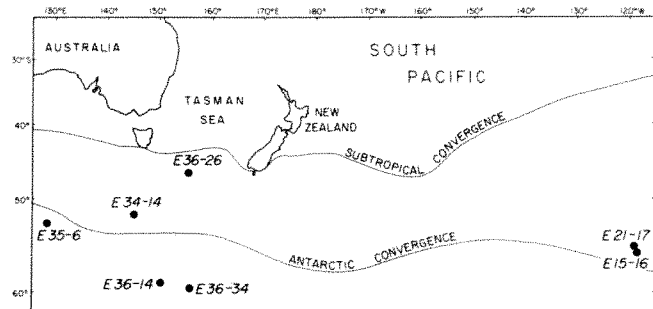


Fig. 1 Map showing location of *Eltanin* cores used in this study and the position of the Antarctic and Subtropical Convergences.

Of the seven cores selected for this study (Fig. 1, Table 1), five are from waters south of Australia (Antarctic waters: E35-6, E36-14, E36-34; Subantarctic waters: E34-14, E36-26) and two are from the central South Pacific (Subantarctic waters: E15-16, E21-17). Four of the five cores south of Australia contain abundant foraminiferal and radiolarian faunas and have palaeoclimatic curves previously established on changes in foraminiferal assemblages². The fifth core, E36-26, has not been previously studied and was selected primarily because it is carbonate free and contains an abundant radiolarian fauna. Subantarctic cores E15-16 and E21-17 have both radiolarian⁹ and foraminiferal¹ palaeoclimatic curves. Two of the seven cores are of Late Pliocene age, and the other five are of Pleistocene age. Palaeomagnetic stratigraphy is available for all the cores^{2,14,15}. For E15-16 and E21-17 the biostratigraphy did

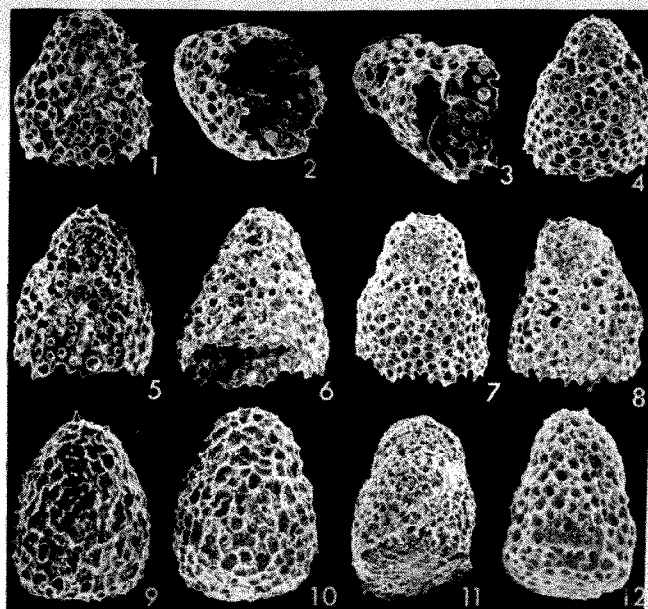


Fig. 2 Nos 1 to 8 *Antarctissa strelkovi* Petrushevskaya: 1, E15-16, 920 to 923 cm, $\times 116$; 2, internal structure, E36-26, 1,222 to 1,224 cm, $\times 107$; 3, internal structure, E36-26, 1,222 to 1,224 cm, $\times 108$; 4, E15-16, 920 to 923 cm, $\times 76$; 5, E21-17, 169 to 171 cm, $\times 92$; 6, E15-16, 920 to 923 cm, $\times 108$; 7, E15-16, 597 to 600 cm, $\times 86$; 8, E21-17, 169 to 171 cm, $\times 88$. Nos. 9 to 12, *Antarctissa denticulata* Petrushevskaya: 9, E36-26, 1,222 to 1,224 cm, $\times 96$; 10, E36-26, 1,222 to 1,224 cm, $\times 84$; 11, showing thoracic plug, E21-17, 169 to 171 cm, $\times 92$; 12, showing thoracic plug, E35-6, 201 to 203 cm, $\times 106$.

not support the palaeomagnetic data, the discrepancy being attributed to the low magnetic intensity in these cores. Thus, the palaeomagnetic stratigraphy for these two cores was inferred from the biostratigraphy¹.

Table 1 Core Parameters

Core	Latitude	Longitude	Water depth (m)	Core length (cm)
E36-26	47° 51' S	155° 05' E	4,691	1,224
E34-14	52° 11' S	145° 03' E	3,264	519
E35-6	53° 12' S	128° 06' E	3,996	600
E21-17	55° 28' S	119° 56' W	2,802	1,004
E15-16	56° 03' S	119° 55' W	3,039	1,200
E36-14	58° 06' S	150° 10' E	3,054	601
E36-34	59° 59' S	155° 02' E	2,794	452

Standard laboratory procedures were followed in the processing of samples and in making faunal slides. Entire slide populations (300 to 1,000 specimens in the $>63 \mu\text{m}$ fraction) were counted for all samples, which were taken at 25 to 40 cm intervals throughout the cores.

Initially, frequency oscillations of *Antarctissa strelkovi* and *Antarctissa denticulata* were investigated. Both forms are consistently abundant throughout the cores. In surface sediments, *A. strelkovi* has its highest frequencies (5% to $>25\%$) in sediments south of 60° S (refs 16 and 17). Petrushevskaya¹⁷ referred to *A. strelkovi* as a high latitude Antarctic species and reported that the distribution of its skeletons in surface sediments of the Southern Ocean corresponds closely with its presence in Antarctic waters. Hays⁴ stated that *A. strelkovi* is probably the most abundant and ubiquitous radiolarian species in the Antarctic, and is the most characteristic species of this fauna. *Antarctissa strelkovi* has also been shown to range from at least the middle of the Gilbert Reversed Epoch to the Recent⁶ ($t=4.0$ m.y. BP to present day). *Antarctissa denticulata* is morphologically similar to *A. strelkovi* and was also

investigated to establish its possible potential as a palaeoclimatic index.

The genus *Antarctissa* is characterised by a compact test, consisting of two segments, the first (cephalis) being somewhat smaller than the second (thorax). The wall of the test has numerous rounded pores, and the surface of the test is generally rough. The internal skeleton consists of

the basic elements typical for nassellarians. *Antarctissa strelkovi* (Fig. 2, Nos 1 to 8) has comparatively thin walls, and the elements of the internal skeleton are more slender and delicate than in *A. denticulata*^{16,17} (Fig. 2, Nos 9 to 12). The massive test of *A. denticulata* has very thick walls, and the thorax is generally closed below by a thick porous plate. The taxonomy and recent distribution of *A. strelkovi*

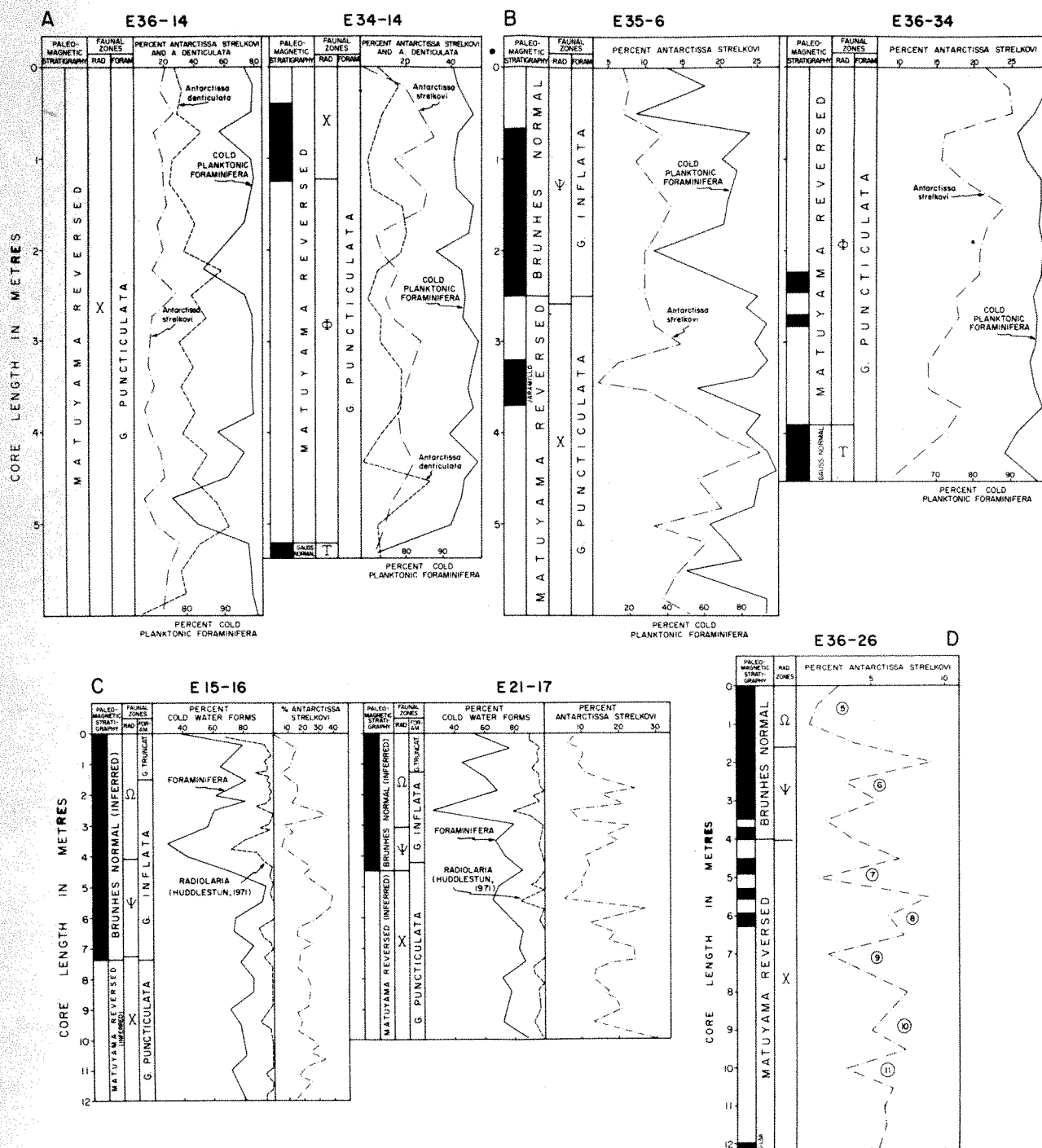


Fig. 3 Comparison of frequency curves of the radiolarian palaeoclimatic index, *Antarctissa strelkovi* with inferred palaeotemperature oscillations in planktonic foraminiferal and radiolarian assemblages in Southern Ocean deep sea cores. A, Comparison of *Antarctissa strelkovi* and *A. denticulata* frequency oscillations with planktonic foraminiferal palaeoclimatic curves², established in two cores of Late Pliocene–Early Pleistocene age south of Australia; B, comparison of *A. strelkovi* frequency oscillations with planktonic foraminiferal palaeoclimatic curves² in two northern Antarctic cores of Late Pliocene–Pleistocene age from south of Australia; C, comparison of *A. strelkovi* frequency oscillations with inferred palaeoclimatic curves based on planktonic foraminifera¹ and Radiolaria⁹ in two Middle to Late Pleistocene cores from the Subantarctic South Pacific; D, frequency oscillations of *A. strelkovi* in a carbonate-free, Early to Middle Pleistocene Subantarctic core. Warm intervals are numbered in accordance with Keany and Kennett². Palaeomagnetic stratigraphy and assigned ages originally given by Watkins and Kennett¹⁴, Kennett¹ and later utilised by Keany and Kennett². Foraminiferal zones after Kennett¹ and Keany and Kennett²; Radiolaria zones (shown by Greek letters) originally defined for the Antarctic area by Hays⁴ and applied to these cores by Kennett¹, Keany and Kennett² and Huddleston⁹.

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and *A. denticulata* are discussed in detail by Petrushevskaya^{16,17}.

My first faunal counts were made on E34-14 and E36-14, differentiating *A. strelkovi*, *A. denticulata* and other species. Although the *A. denticulata* oscillations (Fig. 3A) show no consistent similarity to the foraminiferal palaeoclimatic curve, the curves representing the percentages of *A. strelkovi* are very similar to those palaeoclimatic curves; the colder the temperature, the greater the percentage of *A. strelkovi*. There is a good correlation (Fig. 3B) between the number and amplitude of warm-water peaks indicated by foraminifera and those described in this paper. Good correlation can also be observed in the two central South Pacific cores (Fig. 3C). In these two cores the similarities between the two curves established using Radiolaria are greater than those between the radiolarian and foraminiferal curves, suggesting slightly different ecological responses for Radiolaria and foraminifera. The potential value of the *A. strelkovi* method is emphasised by its oscillations in a carbonate free core, E36-26 (Fig. 3D), which contains sediments of Early Pleistocene age (zone X to zone Ω ^{4,6}). The palaeoclimatic curve determined for this core is consistent with the palaeomagnetically dated palaeoclimatic curve determined for the Southern Ocean using foraminifera².

In cores of Brunhes and Matuyama age, the curves established using fluctuations in *A. strelkovi* support the conclusions of Kennett¹ and Keany and Kennett³ that the Matuyama was, in general, cooler than the Brunhes in Subantarctic and northern Antarctic areas. In the four cores, the percentage of assemblages represented by *A. strelkovi* on average decreases by 26% from the Matuyama Reversed Epoch ($t=2.43$ to 0.69 m.y. BP) to the Brunhes Normal Epoch ($t=0.69$ m.y. BP to present day). In the three cores which contain carbonate sediments of Brunhes and Matuyama age, the boundary between the *Globorotalia inflata* and the *Globorotalia puncticulata* zones¹ occurs within 50 cm above the X- Ψ boundary^{4,6}, therefore coinciding approximately with the Brunhes-Matuyama boundary. Thus, as suggested by Kennett¹, the *G. inflata*-*G. puncticulata* zonal boundary can be used to approximate the Brunhes-Matuyama boundary in carbonate rich cores from the Southern Ocean.

Palaeoclimatic determinations in Southern Ocean cores using the *A. strelkovi* method are limited to the south by the relatively biogenically barren nature of the cores from the Antarctic shelf and to the north by the northern limit of *A. strelkovi*. Cores from the highest latitudes of the Southern Ocean often produce samples containing fifty or fewer Radiolaria, making it difficult to apply radiolarian palaeoclimatic techniques. The scarcity of the radiolarian tests is due to solution of the siliceous tests, dilution by glacial marine sediments and low productivity. In the northernmost core examined (E36-26, 47° 51' S) *A. strelkovi* is less abundant (1 to 9%), and this core probably lies close to the northern limit of the species.

Obvious anomalies in the data occur in two cores. In Antarctic core E35-6, a warm peak at 200 cm suggested by the foraminifera is not as clear in the *A. strelkovi* curve. In Antarctic core E36-14, two very cold episodes indicated by foraminifera at 250 to 375 cm and 600 cm are not reflected by oscillations in *A. strelkovi*.

Determination of oscillations in the frequency of *A. strelkovi* seems to be a valid and rapid approach for palaeoclimatic determinations in the Southern Ocean. Its value is particularly enhanced by the long range of the species from the Pliocene to the Recent and because many Southern Ocean cores are devoid of foraminifera, especially those of Pliocene age.

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Iceland Mantle Plume

O'HARA¹ has objected to my interpretation concerning the trace element chemistry of lavas erupted along the Iceland-Reykjanes Ridge System² on the ground that: (1) Such magmas are not "primary magmas" but residual liquids; (2) instead, such lavas have suffered prior to eruption extensive "gabbro fractionation" at low pressure (olivine-augite-plagioclase extraction), and/or "eclogite fractionation" at higher pressure (clinopyroxene-garnet extraction in a 50-50% mixture); (3) the "extent of fractionation" is directly proportional to the elevation of the surface on which these lavas have been erupted, thus increases toward Iceland, and is the principal cause of trace element variations along the ridge. According to O'Hara, the lavas are derived from a unique and homogeneous mantle at the upper mantle-transition zone boundary and not, as I prefer², from two distinct mantle sources, one forcefully rising as a primary hot mantle plume (PHMP) beneath Iceland and interacting with the depleted low velocity layer (DLVL).

I answer each of these points in order, concentrating primarily on the rare earth (RE) data which I emphasized², and omitting petrological and isotopic arguments, which will be discussed elsewhere.

Also, several of O'Hara's comments concerning rare earth fractionation are, unfortunately, wrong. For example: (i) Fractional crystallization of clinopyroxene does not deplete but rather enriches a residual melt in lighter rare earths, as is evident from equilibrium partition coefficient data³⁻⁵. (ii) There is no relative Y enrichment towards Iceland, because I did not report nor analyse this element, and my expectation is that it will remain relatively constant, similarly to the heavy rare earths of similar ionic size, such as Er. (iii) There is no massive relative and even absolute depletion of Yb as stated by O'Hara to support his eclogite-fractionation model. The Yb abundance remains relatively constant along the ridge up to Iceland (Fig. 1a). Much of the Yb scatter is in fact analytical, as with the

instrumental neutron activation method used the counting statistics are relatively poor for Yb ($\sigma_{Yb}=15\%$, $\sigma_{La}=9\%$, and $\sigma_{Sm}=2.5\%$). (iv) O'Hara's use of the $[La/Yb]_{EF}$ is misleading since it bypasses the behaviour of intermediate rare earths. This ratio does not adequately contrast the behaviour of the light rare earths relative to the heavy rare earth subgrouping. All the information contained in the rare earth pattern needs to be included to constrain the models.

(1) "Primary magmas". This is a semantics problem. I have

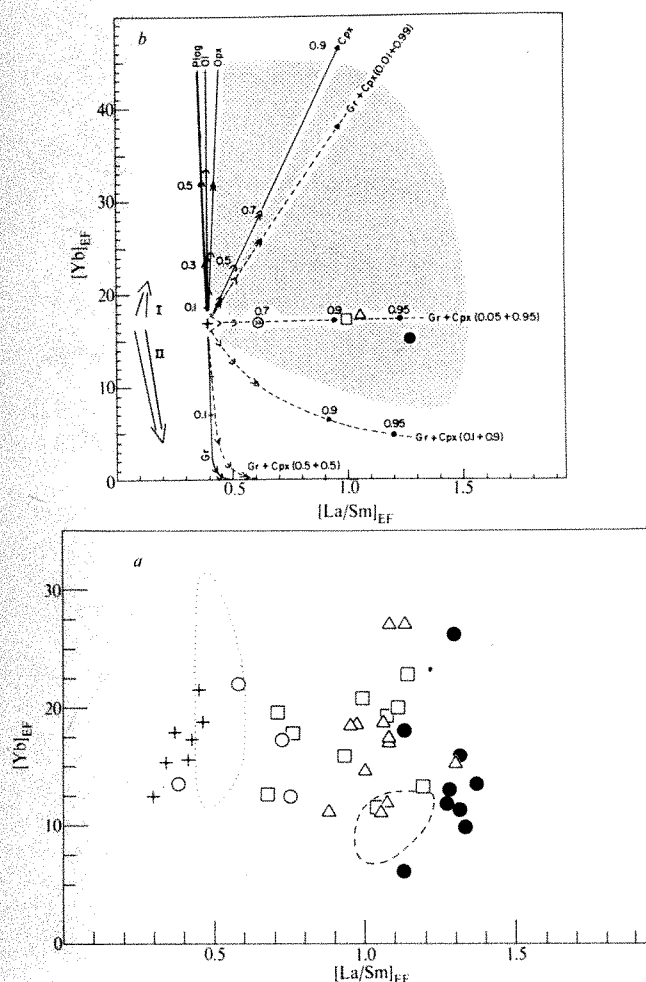


Fig. 1 *a*, Yb against La/Sm enrichment factors relative to chondritic meteorites² in tholeiitic basalts erupted along the postglacial Reykjanes Ridge Axis and its extension over the Middle Neovulcanic Zone of Iceland². +, South of 61°N; ○, 61–62°N; □, 62–63°N; ▤, 63°N to Iceland; ●, Iceland. Dotted area is field of DLVL-derived tholeiitic basalts from other Mid-Ocean Ridges⁶; and dashed area is field for Hawaiian tholeiites³. *b*, Same diagram as above, showing theoretical control liquid lines of descent for fractional crystallization of plagioclase feldspar (Plag), orthopyroxene (Opx), olivine (Ol), clinopyroxene (Cpx) and garnet (Gr). The bar, arrow, half circle, double arrow, filled triangle and point along liquid control lines represent residual liquid composition after fractional crystallisation of respectively 10, 30, 50, 70, 90 and 95 weight % of the corresponding mineral (or bimineralline mixtures for eclogite fractionation—shown as dashed liquid control lines). The large symbols are as given in *a* for the observed values in basalts erupted along the Reykjanes Ridge, but averaged for every degree of latitude. Large arrows: I, the approximate direction of olivine-gabbro fractionation; II, of eclogite fractionation. The lengths are very roughly proportional to the rate of enrichment or depletion for a given degree of fractional crystallisation. Various paths to bridge DLVL-derived melts (+) to PHMP-derived melts (●) can be designed. All these paths require a very unusually large extent of fractional crystallisation of clinopyroxene, and cannot at the same time satisfy the major element chemistry of these two end-member tholeiites (which relative to trace elements represent only small variations). The shaded area takes into account the known range of partition coefficients^{4,8} for plagioclase and the dotted area for the clinopyroxene.

used the adjective "primary" on two occasions to indicate a temporal sequence, where by prior mixing along the transition zone, both PHMP-derived and DLVL-derived melt types are referred as "primary" in contrast to the secondary hybrid lavas resulting from mixing. I did not mean to imply that any of the lavas reported in my paper did not suffer any fractionation prior to eruption, and thus be "primary" in O'Hara's sense. In fact I clearly stated that they are porphyritic in texture, and explained plausible mechanisms by which lavas, once segregated from the residual mantle phases after partial melting during diapiric rise, would accumulate in magma chambers at very shallow depth beneath the thin oceanic crust, cool and begin to fractionally crystallize in order to produce the observed phenocrysts, as well as mix.

Elsewhere⁶ I also used for synonyms⁷ to "primary" the words "principal" melt types, "end-member" melt types, in referring to both PHMP-derived and DLVL-derived tholeiites.

Although we apparently agree that most of these lavas have suffered some crystallization prior to eruption, the question remaining in dispute, I believe, is quantitatively: to what extent are these melts residual, and from what mantle source or sources were they originally derived?

(2) "Olivine-gabbro and eclogite fractionation". I have shown on a $[Yb]_{EF}/[La/Sm]_{EF}$ diagram⁸ the difficulty of bridging by fractional crystallization melts with light RE-depleted pattern (typically mid-ocean ridge basalts, or Reykjanes Ridge south of 61°N) to melts with light RE-enriched pattern (typically island tholeiites, as Iceland), while at the same time keeping $[Yb]_{EF}$ relatively constant. This is shown in Fig. 1*a* and *b*. Only very large amounts of extraction (greater than 90%) of clinopyroxene with rather restricted partition coefficient values (and for that matter also of bulk chemistry) could perhaps bridge both types. This is because operative RE partition coefficients for orthopyroxene, olivine and plagioclase feldspar upon fractional crystallization do not change appreciably the $[La/Sm]_{EF}$ of residual liquids, but merely increase the overall absolute RE abundances (see also Figs 13.15 of ref. 8). Only clinopyroxene is able significantly to fractionate and enrich residual melts in the light RE. On a $[La/Sm]_{EF}/[Yb]_{EF}$ diagram (Fig. 1*b*) the olivine-gabbro liquid-control fractionation line would have to be intermediate between individual controlling lines for plagioclase, olivine and clinopyroxene, and its exact position would depend on the relative proportions of these minerals simultaneously being extracted at the cotectic (see arrow I in Fig. 1*b*). It is clear (Fig. 1*b*) that increasing olivine-gabbro fractionation toward Iceland cannot satisfactorily produce the observed $[La/Sm]_{EF}/[Yb]_{EF}$ variation along the ridge. This, therefore, eliminates one of O'Hara's contentions, that is, an increasing olivine-gabbro fractionation toward Iceland could produce the observed increase of the $[La/Sm]_{EF}$.

So the low pressure olivine-gabbro fractionation can only increase the scatter of $[La/Sm]_{EF}$ towards Iceland, and should be inferred only as a second order effect, as is the eclogite fractionation effect which I now discuss.

Hitherto, I had avoided consideration of the effect of garnet fractionation (although aware of its effect in depleting the heavy rare earths in residual melts having fractionally crystallized garnet⁹) because of the lack of reliable garnet-melt partition data relevant to basalt genesis under eclogitic conditions. In view of O'Hara's remarks, it is necessary to illustrate the control line of liquid descent for eclogite fractionation, using Philpotts's best estimate¹⁰ set of RE partition coefficients for garnet, from the Kakanui region. This set of RE partition coefficient values for garnet gives consistent results with other estimates from other eclogites or garnet peridotites¹⁰. The set is also close to an estimate I had independently made and which is conservative on its effect in depleting the heavy RE. The effect of fractionally crystallizing garnet alone is to deplete drastically the melt in heavy rare earths such as Yb, without changing the $[La/Sm]_{EF}$ appreciably (see Fig. 1*b*). The garnet effect of lowering the $[Yb]_{EF}$ dominates also if garnet and clinopyroxene simultaneously fractionally crystallized from the melt as a 50–50% mixture as

required by O'Hara's eclogite fractionation model¹¹. Again, and contrary to O'Hara's belief, there is no way to match the observed rare earth variation along the Reykjanes Ridge with such an eclogitic fractional crystallization scheme.

Only a mixture composed of 95% clinopyroxene and 5% pyrope garnet could possibly bridge the rare earth pattern variation, but would require some 95% extract of such an unusual mixture. This is of course unacceptable, because the residual liquid of such an extract would have a major element chemistry quite distinct from an olivine tholeiite (the most common lava type over the Reykjanes Peninsula). It would also create a serious volume problem over and above having to explain the two to four times larger flux production of melt in the Iceland Region relative to more normal ridge segments, judging from crustal thickness².

(3) "Extent of fractionation". Although it is true that there is a tendency for increasing fractionation for lava ascending through thicker crust (or altitude), it is untenable that the general trace element geochemical trend observed along the ridge can be accounted for by increasing fractional crystallization alone. As previously noted on the $[La/Sm]_{EF}/[Yb]_{EF}$ diagram, the effect merely increases diversity and scatter about the general trend but cannot be responsible for it. Although at a first glance it may seem that altitude can be correlated with fractionation (such as reflected by the $[La/Sm]_{EF}$), a simple plot of relevant data would show that it is not a regular and simple function. A corollary of my plume model would be that basalt erupted south of 60°N be DLVL-derived and remain light RE-depleted, even though water depth continues generally to increase along the ridge axis. A series of five new rock analyses for stations spaced from 60°N up to the Charlie Gibbs Fracture Zone (~53°N) shows a constant level for the $[La/Sm]_{EF}$ just as south of 61°N (ref. 2, Fig. 3); and therefore further corroborates my model for two mantle sources of different densities and differentiation history.

O'Hara's preferred model of a single mantle source at the upper mantle-transition zone boundary^{11,12} offers little substance for discussion here, as it does not take into consideration the many geophysical-geochemical and geological features which contrast Iceland with the Mid-Atlantic Ridge. I do wish to emphasise that any alternative to my model should also satisfy these many model requirements, which I have listed and have taken into consideration in my model².

Contrary to O'Hara's belief, I rejected the model of a single mantle source with increasing degree of fractional crystallization toward Iceland not only on the basis of isotopic ratios (evidence which for two mantle sources is overwhelming¹³), but also from rare earth considerations as outlined above and which I had to omit in my original discussion² for the sake of brevity.

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Cavitation as a Mechanism for the Synthesis of Natural Diamonds

LET us grant, in accordance with Galimov's proposals¹, that cavitation can occur when flowing magma in a pipe encounters a constriction, and that in the ensuing collapse of a bubble very substantial transient dynamic pressures, of magnitude sufficient to be of thermodynamic importance for diamond synthesis, can be produced. In granting this, we overlook some quantitative details in his calculation, such as the apparent implication that the bubbles would contain gas at 10 or 20 kbar, and yet that their compression (by a factor of 64,000 in volume) can be calculated by ideal gas theory. He ignores the fundamental difference in rate control between martensitic conversion of crystals from one modification to another, which makes a product of the same chemical composition as the starting material, and other processes of crystal growth requiring a composition change. In the former class, to which production of diamond by the action of shock waves on graphite belongs, the limit on growth velocity is essentially the shock wave velocity. Thus, so far as that is concerned, quite a large diamond might be made within a few microseconds. Further characteristics of martensitic processes are, however, that the product takes the form of thin lenses, whereby the constraint by the matrix on shape change in the converting region is minimised and, second, that as a rule there is a multiplicity of orientations of the martensitic product in the parent crystal, so that a microcrystalline product results.

If the product is not to have the same chemical composition as the starting material, time must be allowed for diffusive segregation of chemical constituents. Galimov estimates the duration, t_{coll} , of dynamic pressure due to bubble collapse as 2×10^{-8} s. In this time diffusive segregation could occur through a thickness of order $x = (Dt_{coll})^{1/2}$, where D is the diffusion coefficient. With a fairly generous allowance of $10^{-4} \text{ cm}^2 \text{ s}^{-1}$ for D we have $x \sim 4.5 \mu\text{m}$. The thickness of diamond which could grow from one seed in the given time could not exceed this and would be proportionately less in a medium of low concentration of carbon. Of course, repeated cavitations could give repeated periods of growth, but there is no apparent reason why re-solution would not occur in the much longer intervening periods of diamond instability. Galimov offers no estimate of the carbon content of the medium, except to indicate that 30% is too much. (There are, incidentally, no grounds whatever for his idea that a supersaturated solution of carbon from which diamond could grow would need a carbon concentration of this order of magnitude.)

Thus it is conceivable that some microdiamonds are produced under dynamic pressures due to cavitation in a fast flowing magma, either embedded in graphite or otherwise: and whereas the former might survive it is highly unlikely that the latter would. But it is quite certain that the recognised diamonds for which diamond mines are worked were not produced by this process. These diamonds, of fairly equant habit, and of dimensions of millimetres to centimetres as well as smaller, frequently show inescapable evidence of growth in successive shells on all sides, with discontinuities in the growth conditions, but continuity through thicknesses of tens or hundreds of micrometres, as well as (usually terminal) periods of resolution²⁻⁶. These internal variations of impurity content and texture are readily explained by growth from solutions in times of at least the order of an hour, but quite inexplicable in terms of production by transient dynamic shock pressure.

In brief, the sole basis of Galimov's claim, in connection with his postulated mechanism, that "there are no limitations involving the total concentration of carbon in the medium" is his complete disregard of such limitations, which are inescapable.

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BIOLOGICAL SCIENCES

A Novel Substituted Guanidine with High Activity *in vitro* against Rhinoviruses

THE number and diversity of the viruses which infect the upper respiratory tract, and cause the common cold, virtually preclude the control of this disease by conventional vaccines. From this, apart from symptomatic therapy, the only hope for effective treatment of this most prevalent of diseases is in the development of broad spectrum antiviral drugs. We have developed a substituted guanidine, ICI 65,709 (ref. 1) (Fig. 1) which has good activity *in vitro* against all twenty-five rhinovirus serotypes tested in human embryonic lung cells, and also against certain other picornaviruses.

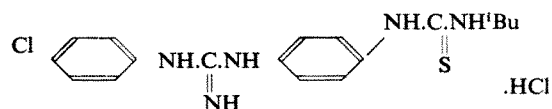


Fig. 1 The structural formula of ICI 65,709; 1-*p*-chlorophenyl-3-(*m* isobutylthioureido) phenyl guanidine hydrochloride.

The method of testing for antiviral activity has been fully described^{2,3}. In brief, it consists of infecting tissue-culture cells in 3×0.5-inch tubes with 100 TCD₅₀ of test virus, and then adding the test compound in a range of concentrations. After incubation at 33° C for 2 d, the cells are inspected with a low power microscope and the concentration of compound which causes 50% cytotoxicity and that which causes 50% inhibition of virus growth (cytopathic effect) are determined. From these values a tissue-culture 'therapeutic ratio' is calculated for each virus tested.

Table 1 shows that although the range of viruses tested was limited, it is clear that the activity of the compound is not confined to the rhinoviruses. Certain other picornaviruses were sensitive, and there was also some activity against vaccinia, herpes simplex, and the two arboviruses tested. The compound was inactive against equine rhinovirus, respiratory

syncytial virus and the 229E strain of coronavirus, and also against influenza or parainfluenza grown in calf kidney cells.

A curious feature of the compound was that its antiviral action was highly dependent on the type of cell in which it is tested. For example, although the growth of rhinovirus type 2 in human embryonic lung cells is strongly inhibited by ICI 65,709, the same virus grown in KB cells, HeLa or primary rhesus monkey kidney cells is completely insensitive to the compound. When rhinoviruses are grown in fragments of human embryonic trachea, 1 μg ml⁻¹ ICI 65,709 inhibits growth by approximately 90%.

Table 1 50% Toxic and 50% Antiviral Concentrations of ICI 65,709 Against Various Viruses

Cell type	50% toxic concentration (μg ml ⁻¹)	Virus	50% antiviral concentration (μg ml ⁻¹)	Therapeutic ratio <i>in vitro</i>
Human embryonic	6	Rhinovirus type 6, 5, 35	0.4	15
		33, 3, 44, 40, 1A, 9, 43	0.2	30
		32, 14, 29, 27, 11, 1B, 2	0.1	60
		15, 16, 31, 4, 26, 36, 17	0.05	120
		Equine rhinovirus	Not active	—
		Echovirus type 11	0.05	120
		14	0.1	60
		Coxsackie virus type A9	0.4	15
		A21 (Coe)	0.8	7
		B3	0.1	60
		Vaccinia	0.2	30
		Herpes viruses:		
		H. simplex type 1	1.0	6
		H. simplex type 2	1.0	6
		Pseudorabies	Not active	—
Primary calf kidney	12	Semliki forest	0.8	7
		Sindbis	0.8	7
		Influenza A ₀	Not active	—
		A ₁	Not active	—
		A ₂	Not active	—
		Parainfluenza 1	Not active	—
		Respiratory syncytial	Not active	—
		Coronavirus 229E	Not active	—

Studies on the mode of action of ICI 65,709 using rhinovirus type 2 in human embryonic lung cells have shown that the compound does not destroy the rhinovirus virion, nor does it prevent the attachment or penetration of virus particles into the host cell. When the compound is added to virus-infected cells at various times after infection, and the virus yields at the end of the first growth cycle are measured, the compound is seen to exert progressively more inhibition of virus growth the longer it is present on the infected cell. This suggests an effect on a virus synthetic process which begins soon after eclipse and continues throughout the replicative process: possibly virus RNA or protein synthesis. The compound has no inhibitory effect on the RNA or protein synthesis of the host cell at concentrations up to 100 times the 50% antiviral level.

Although ICI 65,709 is a derivative of guanidine, its antiviral action differs from that of guanidine⁴ in at least two ways. First, it does not give rise to drug-resistance as does guanidine, and second, its action is not reversed by substances such as ethanolamine, choline, methionine, or lactalbumin hydrolysate⁵⁻⁸. Biochemical studies (Kolias, S. I., and Dim-

mock, N. J., unpublished) also suggest that ICI 65,709 differs in its mode of action from guanidine.

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C-reactive Protein-like Precipitins in Plaice

C-REACTIVE protein (CRP) is an acute phase protein appearing in the serum of man during the febrile stage of infections with pneumococci and various other microorganisms^{1,2}. The protein can also be detected in serum and other serous fluids during pathological conditions in which tissue injury, inflammation or carcinoma are involved^{3,4}. Acute phase proteins have also been detected in the sera of a number of other vertebrates, including monkeys, rabbits and mice⁵, but there seem to be few reports of these proteins in lower vertebrates⁶.

In the presence of Ca²⁺, CRP is precipitated from solution by pneumococcal C-substance^{1,7} and also by extracts from a number of fungi, invertebrates and plants⁸⁻¹⁰. Following the demonstration that various phosphate monoesters inhibit the CRP-C-polysaccharide precipitation reaction¹¹, phosphorylcholine has recently been found to be the most active inhibitor of all the compounds so far tested¹².

Using extracts from *Diplococcus pneumoniae*, some fungi and a nematode, *Ascaris lumbricoides*, together with a peptido-polysaccharide isolated from the dermatophyte *Epidermophyton floccosum*, we have found a CRP-like serum component in the plaice (*Pleuronectes platessa* L.), a marine teleost. We describe here specificity studies carried out with the plaice precipitin and discuss the origin and possible biological role of such proteins in poikilotherms.

Fish were caught in shallow water off the coast of Aberdeen and transferred to aerated seawater at 11–14° C in the aquarium. Single serum samples were collected¹³ between 1 h and 4 months after the capture of the fish. Human serum containing CRP was obtained from the Brompton Hospital, London, from patients with pulmonary diseases. The presence of CRP in the human samples was established by precipitation with rabbit anti-CRP (Behringwerke). Aqueous extracts of *D. pneumoniae*, *E. floccosum*, *Aspergillus flavus*, *Aspergillus fumigatus*, *Trichophyton mentagrophytes*, *T. rubrum* and *A. lumbricoides* were prepared from culture filtrates and minced worms by methods already described^{1,8,14}.

Precipitation studies with con A have shown that this reagent reacts with polysaccharides from a variety of fungi including *E. floccosum* and a number of *Aspergillus* and *Trichophyton* species

(B. A. B. and J. Pepys, unpublished). A peptido-polysaccharide was isolated from *E. floccosum* by passage of the aqueous extract through a column of Sepharose-con A (Pharmacia) and elution of the adsorbed material with 0.1 M α -methyl-mannopyranoside in physiological saline. After dialysis and lyophilisation, the peptido-polysaccharide was used in precipitation studies.

Forty-four of forty-seven different plaice sera examined (from thirty males and females of approximately 2 to 7 yr and seventeen O-group plaice) precipitated in gel with *E. floccosum* extract. The sera also precipitated with the peptido-polysaccharide and the lines were completely confluent with those formed with culture filtrate extracts from the five fungi examined and extracts from *A. lumbricoides* and *D. pneumoniae*. The precipitin reactions observed when plaice serum and human CRP-containing serum were examined in gel diffusion experiments with some of the extracts are shown (Fig. 1a and b). As with the plaice serum, the human serum formed a continuous line of precipitation with all of the extracts. When the plaice and human sera were examined side by side in gel with *E. floccosum* peptido-polysaccharide, *E. floccosum* culture filtrate extract and pneumococcus extract, precipitation occurred in front of each of the peripheral wells and the precipitin lines merged with no sign of spurring (Fig. 1c).

Our evidence supports the view that the precipitins in the plaice sera are not antibodies. Immersion of the gels in 5% sodium citrate or 0.1 M EDTA in physiological saline caused the disappearance, within 30 min, of the lines between the plaice serum and human CRP and the pneumococcus, fungal and *Ascaris* extracts. In contrast, citrate or EDTA did not affect the precipitin reaction observed between *Vibrio anguillarum* extract and serum from a plaice previously immunised with this antigen¹⁵. Immunoelectrophoresis of whole plaice serum in Ionagar at pH 8.6 followed by development against *E. floccosum* culture filtrate extract or peptido-polysaccharide revealed a precipitin line in the α_2 -region, and antibody activity was associated with an immunoglobulin migrating in the β -region. The plaice and human CRP precipitin lines were dissolved within 2 h after immersion of the gels in 0.001 M phosphorylcholine in physiological saline. The lines were not soluble in 0.002 M solutions of choline chloride, α -D-glycerophosphate, AMP, CMP, UMP, glucose-1-phosphate, glucose-6-phosphate or in phosphate-buffered saline. Precipitation of plaice serum with *E. floccosum* peptido-polysaccharide and inhibition of this reaction with phosphorylcholine was confirmed with quantitative studies. In a typical experiment (Table 1), 200 μ l of plaice serum produced maximum precipitation (2.6 μ g of protein N) with 1,086 μ g of *E. floccosum* peptido-polysaccharide. Using these quantities of reagents, inhibition studies revealed that precipitation could be partially inhibited (76%) by 1 μ mol of phosphorylcholine and completely inhibited by 10 μ mol.

Table 1 Precipitation of *Epidermophyton floccosum* Peptidopolysaccharide by Plaice Serum

Peptido-polysaccharide used (μ g)	N in precipitate (μ g)
108.6	0.42
217.2	0.76
543.0	1.90
760.2	2.30
1,086.0	2.55
1,303.2	2.42

Quantitative precipitin analysis was carried out using a micro-precipitin technique and ninhydrin procedure for nitrogen determination²¹. Volume of serum per tube, 200 μ l. Total volume, 350 μ l.

The finding of CRP-like precipitins in the sera of apparently healthy male, female and young plaice, together with the fact that these precipitins were detected in almost all of the fish examined, suggests that this protein may be a normal component of plaice serum and not arise, as in higher vertebrates, only after infection or trauma. Some of the plaice examined had been in the aquarium for 4 months and were feeding

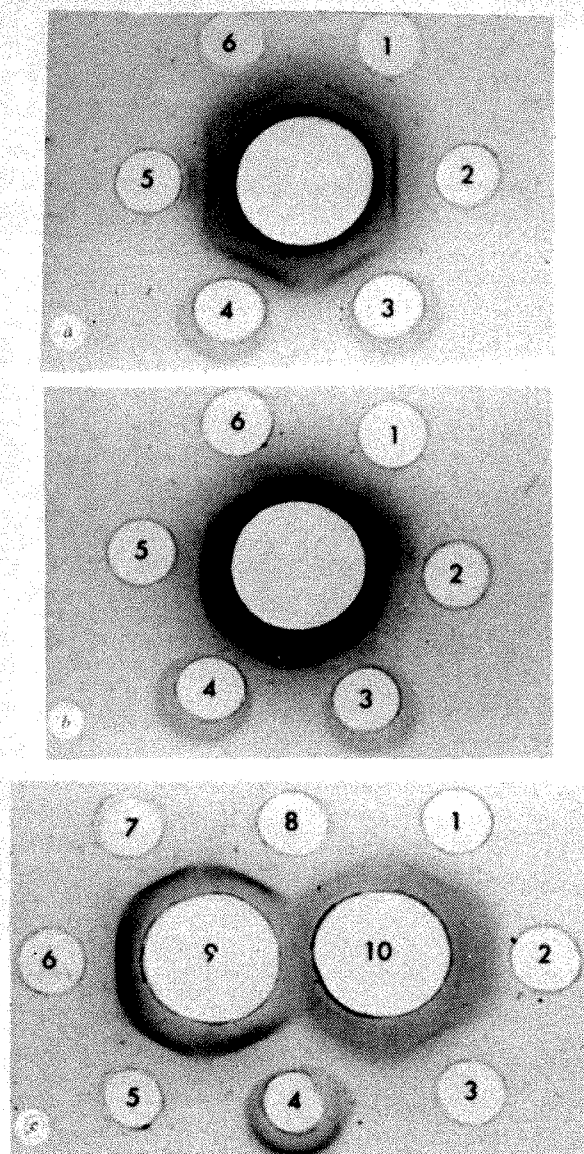


Fig. 1 Agar gel diffusion patterns formed from the reactions of plaice serum and human serum containing C-reactive protein with extracts from some fungi, *Ascaris lumbricoides* and *Diplococcus pneumoniae*. *a*, Centre well, plaice serum; peripheral wells, 1, *E. floccosum* peptido-polysaccharide 10 mg ml⁻¹; 2, *E. floccosum* extract 20 mg ml⁻¹; 3, *A. lumbricoides* extract 20 mg ml⁻¹; 4, *A. fumigatus* extract 20 mg ml⁻¹; 5, *T. mentagrophytes* extract 20 mg ml⁻¹; 6, *E. floccosum* peptido-polysaccharide 10 mg ml⁻¹. *b*, Centre well, human serum containing C-reactive protein; peripheral wells as for *a*. *c*, Peripheral wells 1, 3, 5, and 7, *E. floccosum* extract 23 mg ml⁻¹; 2, 6, *D. pneumoniae* extract 20 mg ml⁻¹; 4, 8, *E. floccosum* peptido-polysaccharide 11 mg ml⁻¹. Centre wells, 9, human serum containing C-reactive protein; 10, plaice serum.

regularly, which would suggest that they had recovered from the possible initial trauma of capture. Our preliminary studies have shown that sera from dab (*Limanda limanda* (L.)) and cod (*Gadus morrhua* L.) also contain fungal precipitins soluble in 5% sodium citrate solution. Specificity studies on these precipitins are in progress.

The ability of poikilotherms to mount a potent antibody response is now well established¹⁵ but it is also clear that antibody production is often restricted at low temperatures^{16,17}. In its natural environment the plaice is commonly found at temperatures of 10° C and below and at these lower temperatures non-antibody precipitins might provide a valuable adjunct to the animal's defences against infection. In these circumstances it would be advantageous for primitive vertebrates to have

serum proteins with broad specificity for determinants commonly found in the cell walls or surface structures of invading organisms. Phosphorylcholine may be such a widely occurring determinant as its presence in antigens from a number of bacteria, fungi and parasites has recently been suggested by precipitation results obtained with mouse anti-phosphorylcholine myeloma proteins^{18,19}. The possibility therefore exists that non-antibody precipitins form part of the fishes' humoral defences against invasion by microorganisms and parasites. Evidence of a possible anti-bacterial role for human CRP has recently been presented²⁰.

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Inhibition of Local Graft-versus-Host Reaction by Anti-Alloantibodies

THE variable part of an antibody molecule can be used as an antigen within the species that produces it. Antibodies against such variable part antigenic determinants (idiotypes) are called anti-idiotypic¹. One example of anti-idiotypic antibodies is found in alloantibody systems, where A anti-B antibodies directed against histocompatibility antigens can be shown to elicit the formation of anti-alloantibodies when injected into (A × B) F₁ hybrids^{2,3}. That the hybrid indeed synthesises anti-alloantibodies has been demonstrated both by studies on the kinetics of formation⁴ and on the allotypic specificity⁵ of the F₁ product. Such anti-alloantibodies can be shown to

react not only with humoral alloantibodies³, but also with cells carrying receptors (recognition structures) of the same idiotype specificity². The possibility of using anti-alloantibodies for highly selective immunosuppression of transplantation reactions *in vivo* is of obvious importance. We have therefore attempted to prevent a local graft-versus-host (GvH) reaction in rats by anti-alloantibody.

Rats of the inbred strains Lewis and DA, differing at a major histocompatibility locus⁶, and their hybrids were used. Lewis anti-DA and DA anti-Lewis alloantisera were obtained 24 d after grafting DA skin on Lewis hosts and *vice versa*. These sera served to immunize two groups of 5 to 8 week old (Lewis × DA) F₁ animals. Each animal received five intradermal injections of 0.2 ml of alloantiserum in the skin of its belly on day 0, and 1.0 ml of the same alloantiserum intraperitoneally on day 14. An average of 2 ml of blood was obtained from half of the animals in each group on day 21, to be used later in passive immunisation experiments. Later on the same day 5 × 10⁶ viable normal Lewis spleen and lymph node cells were injected into one hind foot, and the same numbers of DA lymphoid cells were injected into the other hind foot of each immunised F₁ hybrid. 7 d later, the popliteal lymph nodes were excised and weighed⁷.

Table 1 Weights (mg) of Popliteal Lymph Nodes of (Lewis × DA) F₁ Rats Actively Immunized with Lewis Anti-DA Alloantibody

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
12.35	82.00	0.15	-0.361 ± 0.041 *
26.84	98.32	0.27	
26.89	95.56	0.28	
24.22	82.00	0.30	
31.57	99.23	0.32	
26.27	75.54	0.35	
50.42	123.61	0.41	
35.57	86.49	0.41	
31.01	75.03	0.41	
49.25	114.93	0.43	
38.21	87.02	0.44	
53.52	117.51	0.46	
33.38	73.00	0.46	
34.22	67.48	0.51	
44.31	79.43	0.56	
64.00	105.29	0.61	
67.30	95.66	0.70	
43.92	62.09	0.71	
33.18	42.33	0.78	
48.27	58.46	0.83	

Viable lymphoid cells from strains Lewis and DA were injected into opposite feet. The corresponding popliteal lymph nodes were excised 7 d later.

* Significantly different from 0 ($P \leq 0.01$).

Table 1 shows that in F₁ animals immunised with Lewis anti-DA the node responding to the injection of Lewis cells was significantly smaller than the node corresponding to the injection of DA cells. Conversely, in animals immunised with DA anti-Lewis, the DA node was smaller than the Lewis node (Table 2). Non-stimulated lymph nodes in rats of the same age, however, averaged 7 mg and were thus considerably smaller than the "inhibited" nodes in Tables 1 and 2, indicating that this inhibition was relative but not complete.

We concluded from this experiment that in animals actively immunised with alloantibody, the GvH reaction induced by parental lymphoid cells was specifically reduced by anti-alloantibody. Other interpretations, however, might be offered. It could be argued that the injected A anti-B alloantibody itself covered certain antigenic B sites in the F₁ host, thereby impeding stimulation of A cells by these antigens.

To test this alternative hypothesis, passive immunisation with variously absorbed anti-alloantisera was arranged. Serum pools obtained from the immunised F₁ animals used in the first experiment will be referred to as anti-(Lewis anti-DA) (Table 3) and anti-(DA anti-Lewis) (Table 4), respectively.

Both sera were twice absorbed with 20 × 10⁶ (Lewis × DA) F₁ lymphoid cells ml⁻¹ to eliminate possible remnants of the alloantibodies used to immunize the animals. Each serum was then subdivided into three parts of 4 ml each. One part was left untreated, A, the other part was absorbed three times with 20 × 10⁶ Lewis lymphoid cells ml⁻¹ for 15 min, B, and the third part was similarly absorbed with DA lymphoid cells, C. Each sample was then injected intraperitoneally into four normal (Lewis × DA) F₁ hosts (1 ml per rat). Four hours later, 5 × 10⁶ viable parental lymphoid cells were injected into the hind feet of each passively immunised animal, as done in the first experiment. After 7 d, the popliteal nodes were excised and weighed.

Table 2 Weights (mg) of Popliteal Lymph Nodes from (Lewis × DA) F₁ Rats Actively Immunized with DA Anti-Lewis Alloantibody

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
72.40	73.34	0.99	0.240 ± 0.047 *
59.00	54.34	1.09	
80.20	71.62	1.12	
44.38	37.86	1.17	
60.60	49.88	1.21	
48.31	36.39	1.33	
75.01	52.79	1.42	
69.20	48.24	1.43	
86.76	61.03	1.44	
89.21	62.00	1.44	
61.30	34.85	1.76	
59.33	33.44	1.77	
94.13	53.30	1.77	
55.04	30.09	1.83	
72.50	36.65	1.98	
81.48	33.58	2.43	
72.31	22.18	3.26	
82.51	22.41	3.68	
100.22	15.00	6.68	

Viable lymphoid cells from strains Lewis and DA were injected into opposite feet. The corresponding popliteal lymph nodes were excised 7 d later.

* Significantly different from 0 ($P \leq 0.01$).

Table 3 Weights (mg) of Popliteal Lymph Nodes of (Lewis × DA) F₁ Rats Receiving Anti-idiotypic Antibodies made in (Lewis × DA) F₁ Rats Against Lewis Anti-DA Alloantibodies

A, F₁ animals passively immunised with anti-(Lewis anti-DA) absorbed with F₁ cells only.

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
17.16	124.00	0.14	-0.508 ± 0.184 *
15.74	98.29	0.16	
66.25	108.75	0.61	
68.09	99.75	0.68	

B, F₁ animals passively immunised with anti-(Lewis anti-DA) absorbed with F₁ cells and with Lewis cells.

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
92.98	105.24	0.88	0.035 ± 0.043 †
76.15	76.32	1.00	
89.40	77.69	1.15	
119.48	87.16	1.37	

C, F₁ animals passively immunised with anti-(Lewis anti-DA) absorbed with F₁ cells and with DA cells.

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
52.43	101.54	0.52	-0.187 ± 0.034 *
81.57	120.45	0.68	
59.25	86.58	0.68	
56.40	76.61	0.74	

Viable lymphoid cells from strains Lewis and DA were injected into opposite feet. The corresponding popliteal lymph nodes were excised 7 d later.

* Not significantly different from Table 1; significantly different from 0 ($P < 0.05$).

† Not significantly different from 0; significantly different from Table 1 ($P < 0.05$).

Tables 3 and 4 show that the inhibition of GvH reactivity could be passively transferred with antiserum, even though this serum had been obtained from F₁ animals and had, in addition, been absorbed with F₁ cells and was thus presumably free of the last traces of the originally injected alloantibody (groups A of Tables 3 and 4).

Comparison of groups A in Tables 3 and 4 with Tables 1 and 2 shows that passive immunisation led to lymph node weight ratios not significantly different from those obtained in actively immunised rats. Absorption with cells from the strain against which the original alloantibody was directed (Table 3C and Table 4B) likewise failed to produce a significant change in weight ratio from that of actively immunised rats. In contrast, absorption with lymphoid cells from the strain which had produced the alloantibody abolished the inhibitory activity, making the mean lymph node weight ratios (Tables 3B and 4C) close to one. Such a ratio of one is found in the present strain combinations when using the same number of normal parental cells into normal F₁ hybrid recipients. This, then, must mean that the lymphoid cells used for absorption in Tables 3B and 4C carried receptors of the same idotype as the humoral alloantibody.

We interpret these findings in the following manner. Inhibition of the local GvH reaction by anti-alloantibodies cannot be explained in terms of residual alloantibody coating relevant target sites. Rather, an effect on the specific receptors for antigen on the parental lymphoid cells has to be envisaged. It is therefore likely that circulating alloantibodies induced by an allogeneic skin graft and certain receptors active in local GvH reaction share idotypic determinants.

Our data support and extend the finding that a lethal GvH disease could be prevented by antiserum directed at recognition structures of attacking cells⁸. "Selective immunological disarmament"⁹ would thus seem to be feasible *in vivo*. This is also confirmed by two recent abstracts^{10,11} and by unpublished observations (S. Zakarian, personal communication).

Table 4 Weights (mg) of Popliteal Lymph Nodes of (Lewis × DA) F₁ Rats Receiving Anti-idiotypic Antibodies made in (Lewis × DA) F₁ Rats Against DA Anti-Lewis Alloantibodies

A, F₁ animals passively immunised with anti-(DA anti-Lewis) absorbed with F₁ cells only.

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
90.09	63.66	1.41	0.299 ± 0.060 *
110.13	61.43	1.79	
131.05	52.83	2.48	
127.73	51.29	2.49	

B, F₁ animals passively immunised with anti-(DA anti-Lewis) absorbed with F₁ cells and with Lewis cells.

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
87.21	78.86	1.11	0.115 ± 0.033 *
90.76	73.54	1.24	
87.25	64.79	1.35	
94.48	60.64	1.56	

C, F₁ animals passively immunised with anti-(DA anti-Lewis) absorbed with F₁ cells and with DA cells.

Lewis node	DA node	Ratio Lewis/DA	Mean log ratio ± s.e.
88.07	120.49	0.73	0.007 ± 0.056 †
126.51	129.67	0.98	
116.70	105.26	1.11	
129.37	96.30	1.34	

Viable lymphoid cells from strains Lewis and DA were injected into opposite feet. The corresponding popliteal lymph nodes were excised 7 d later.

* Not significantly different from Table 2; significantly different from 0 ($P < 0.05$).

† Not significantly different from 0; significantly different from Table 2 ($P < 0.05$).

Finally, from the present data we cannot decide whether B and T cells reactive against the same histocompatibility antigens use receptors of the same idotype. Purified B and T cell populations will have to be used to decide the issue. Meanwhile all that can be said is that the local popliteal lymph node assay has been considered to measure in a rather exclusive manner the reactivity of specific T cells⁷.

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Differential Staining of Nucleolus Organisers in Mammalian Chromosomes

THE *in situ* DNA-RNA hybridisation techniques to locate a certain genome fraction with unique nucleotide sequences¹⁻⁶ have assigned ribosomal cistrons to the satellites of human D and G group chromosomes^{4,5}. This is of particular interest because the satellites organise nucleoli in somatic⁷ and meiotic cells⁸⁻¹⁰. During the course of study on the Giemsa banding mechanism (unpublished) we found that the satellite bodies of human acrocentrics can be differentially stained with Giemsa after simple procedures including extraction of both nucleic acids and histones. The staining profile, herein referred to as 'N band', differed clearly from the Quinacrine, Giemsa, Reversed-Giemsa, Centromeric, or Giemsa 11 banding patterns^{11,12}. In rat kangaroo chromosomes, the N bands appeared exclusively in the nucleolus organisers^{13,14}, that is, in the secondary constriction of the X chromosome. Further application of this technique to other mammalian species strongly indicated that the N-band-positive sites coincide with nucleolus organisers.

Air-dried or flame-dried chromosome slides were prepared from various cell sources: cultured human lymphocytes, a subline of the rat kangaroo (*Potorous tridactylus*) cell line Pt-K₁, an Indian muntjac (*Muntiacus muntjak*) cell line KLS (established in our laboratory), rat (*Rattus norvegicus*) lung fibroblasts, a Chinese hamster (*Cricetulus griseus*) cell line DON, monkey (*Macaca fascicularis*) lung fibroblasts, embryonic mouse (*Mus musculus*) cells and mouse testis

cells^{15,16}. The slides were incubated in 5% trichloroacetic acid (TCA) for 30 min at 85–90° C, briefly rinsed in tap water, and reincubated for 30–45 min at 60° C in 0.1 N HCl. The slides were then thoroughly rinsed in tap water and stained for 60 min with phosphate-buffered Giemsa (diluted 1:10), pH 7.0. Digestion of chromosomes with DNase (100 $\mu\text{g ml}^{-1}$ for 60 min at 37° C at pH 6.6) and RNase (pancreatic RNase A; 100 $\mu\text{g ml}^{-1}$ for 60 min at 37° C at pH 7.0) could be substituted for the TCA step.

In well spread human metaphase plates, the N bands appeared as distinctive purplish red spots restricted to the satellite regions of all acrocentric chromosomes (Fig. 1), whereas no such deeply stained bands were observed in any other chromosome or chromosomal region including the secondary constrictions of chromosomes 1, 9 and 16. Application of the Quinacrine staining method¹⁷ before the N staining showed unequivocally that N bands were located exclusively on the satellites but not on the centromeres, short arms or stalks of satellites (Fig. 2a, b). It was obvious that even negatively or faintly fluorescent satellites could be visualised by the present technique. Although two N-band spots on each acrocentric were usual (Fig. 2b), they were frequently fused to form one spot (Fig. 1). The variation in size and number of N bands in different acrocentric members as well as in different individuals apparently reflects the genetic polymorphism which may serve as an excellent genetic marker. On the other hand, in almost all nuclei of interphase human lymphocytes the N bands appeared as tiny spots clustering within the nucleoli (Fig. 3a). Such clustering was conspicuous until late prophase when the chromosomes began metaphasic orientation (Fig. 3b).

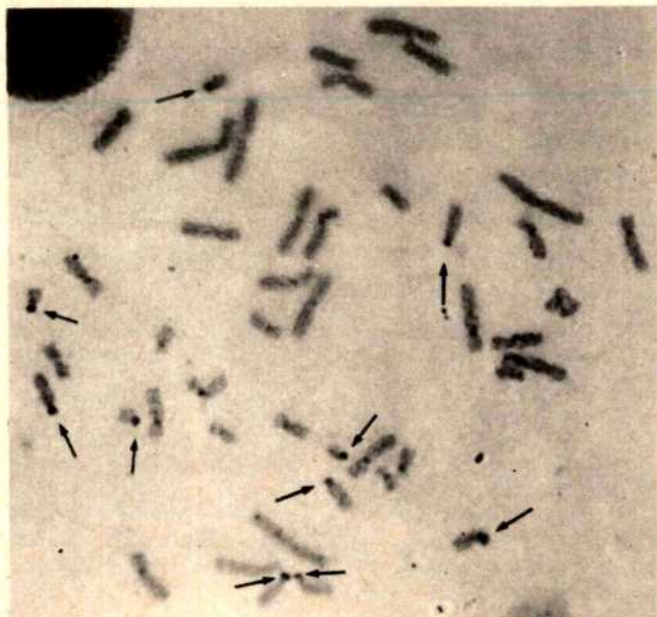


Fig. 1 Metaphase chromosomes of a human male shown by the N-staining method.

In the rat kangaroo metaphase chromosomes, N bands were clearly visible at the secondary constriction of the X chromosomes (Fig. 4a), apparently coinciding with the nucleolus organisers^{13,14}. Indian muntjac and monkey chromosomes were also tested, as they have conspicuous secondary constrictions in certain chromosomes^{18–20}. Although their nucleolus organisers have not been located in prophase nuclei, the exclusive detection of N bands in the secondary constrictions (Fig. 4b) and interphase nucleoli was notable. In the rat and Chinese hamster chromosomes the telomeric ends and centromeres of certain bi-armed and telocentric elements were shown to be nucleolus organisers

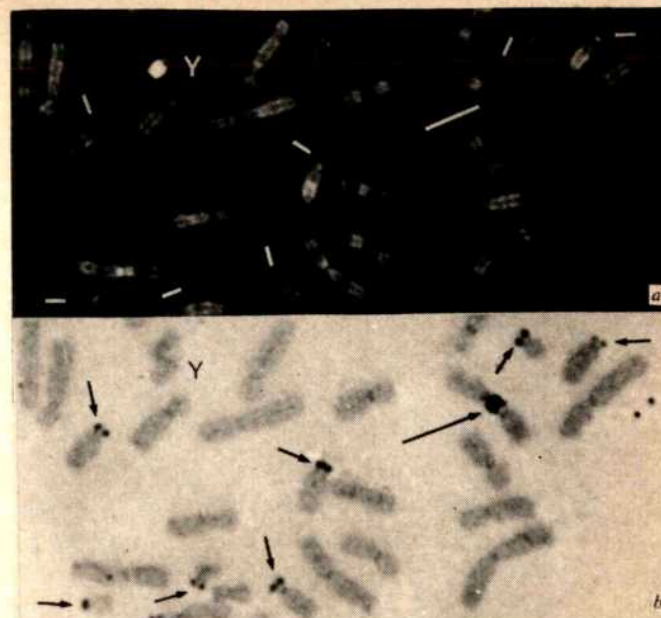


Fig. 2 A partial male karyotype of man, by Quinacrine staining (a) and N-staining (b) methods. A satellite association (upper right, b) is clearly demonstrated (long arrow).

in the prophase nuclei, as in other species^{13,21}, and to be N-band-positive. In the mouse chromosomes, however, the N band was similar in appearance to the C band, though the former appeared to be smaller and located at the centromeric end (Fig. 4c). In Sertoli cells of the mouse testis, the C-band-positive heterochromatins²² were entirely N-band-negative (Fig. 4d). As in the case of human cells, interphase cells of all the animals tested here showed deeply stained N-band figures clustering exclusively within the nucleoli. The above observations strongly suggest that in these animals all N-band-positive sites coincide with nucleolus organisers.

Since our technique was devised to extract both nucleic acids and histones in histological preparations²³, the N-band substances were thought to be acidic proteins. This was supported by several tests. First, chromosomes treated with TCA and HCl were all negative for Feulgen, methyl green-pyronin, alkaline fast green (pH 8.0)²⁴, ammoniacal silver²⁵ and PAS stainings. Second, chromosomes digested with proteolytic enzymes such as Pronase (Kaken, Tokyo; 100 $\mu\text{g ml}^{-1}$ for 10 min at 37° C) or trypsin (Sigma; three times crystallised; 10 $\mu\text{g ml}^{-1}$ for 10 min at 37° C) did not show the N band. Third, treatment with 0.1 N NaOH for 1 min

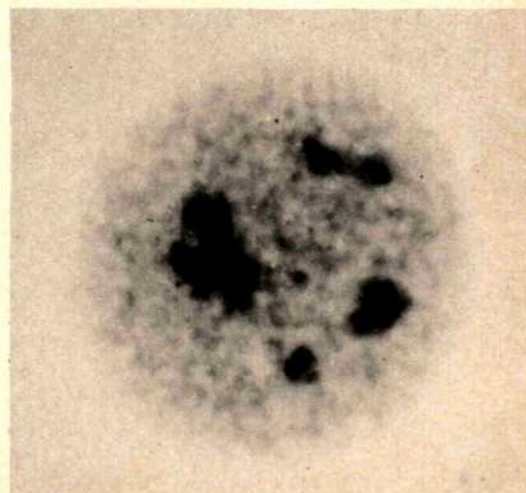


Fig. 3 Cultured human interphase lymphocyte stained by the N-banding method.

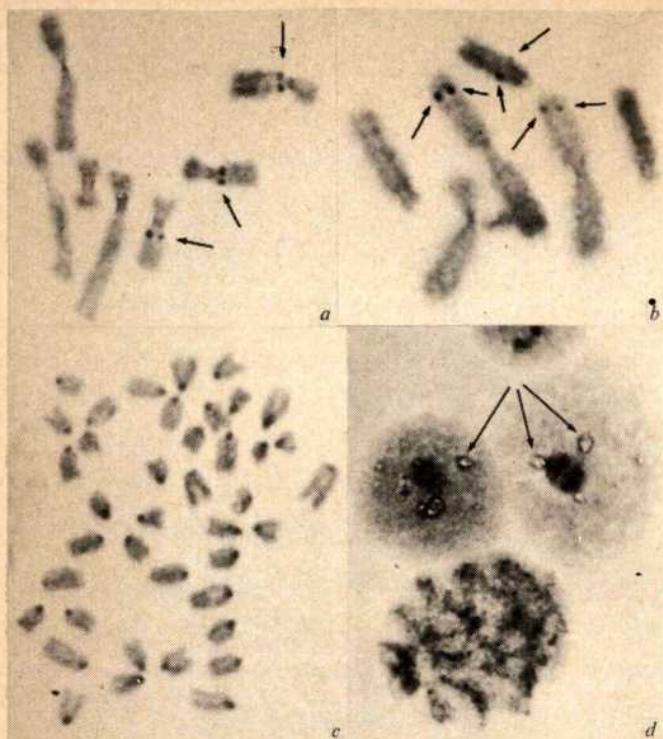


Fig. 4 N bands from: *a*, rat kangaroo (partial metaphase of a triploid subline of Pt-K₁ with three X chromosomes); *b*, Indian muntjac; *c*, embryonic cell of the mouse; *d*, mouse testis, showing negatively stained C bands in Sertoli cells (arrowed). The N-band cluster is obvious in the nucleoli.

after the TCA and HCl steps abolished N-band staining, whereas treatment with 0.2 N H₂SO₄ after the TCA and HCl steps did not change N-band staining.

Although the mechanism involved in the N-staining procedure remains uncertain, it is interesting that acidic proteins may be involved in the expression of ribosomal cistrons in mammalian nuclei. N bands may provide useful genetic markers, and we are investigating further their cytogenetic and biochemical properties.

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Why Centric Regions of Quinacrine-treated Mouse Chromosomes show Diminished Fluorescence

Rowley and Bodmer¹ reported that the centric regions of quinacrine-treated mouse chromosome preparations show less fluorescence intensity than the remainder of the chromosome. They argued that because these centric regions contain a type of DNA that is richer in AT base pairs than unique sequence DNA, they would be expected to show diminished fluorescence according to the model proposed by Caspersson *et al.*², according to which localised quinacrine fluorescence was attributed to the preferential binding of quinacrine mustard to the N-7 position of guanylyl residues in DNA. Thus, one would expect a relative paucity of guanylyl residues in the DNA of the centric regions to be associated with diminished fluorescence. It has since been shown^{3,4} that enhanced quinacrine fluorescence is due to AT base pairs, and studies of a series of GC-containing DNA polymers indicated that GC base pairs (or G alone) actually quenched fluorescence⁴. These observations did not explain why the centric regions of mouse chromosomes with their relatively greater abundance of AT base pairs show diminished quinacrine fluorescence.

Table 1 Effect of DNA Polymers on Quinacrine Fluorescence

DNA polymer added	mol % G+C	Fluorescence	Fold over control
None	—	35	0
(dA) _n ·(dT) _n	0	85	+1.4
(dG) _n ·(dC) _n	100	10	-0.7
(dA) _n ·(dT) _n + (dG) _n ·(dC) _n (1:1 mixture)	50	55	+0.6
<i>E. coli</i> DNA	52	5	-0.9
<i>C. perfringens</i> DNA	32	30	-0.1

DNA polymers (10⁻⁴ M, phosphate basis) were mixed with quinacrine (2 × 10⁻⁶ M) in 0.1 M (Na) phosphate buffer, pH 6.8. Excitation was at 425 nm and fluorescence was measured at 490 nm.

To answer this question we examined further fluorometric properties of quinacrine in the presence of DNA polymers (Table 1). (dA)_n·(dT)_n enhances quinacrine fluorescence while (dG)_n·(dC)_n quenches fluorescence. A 1:1 mixture prepared by mixing equal volumes of these two samples still enhances fluorescence but with diminished efficiency, presumably due to dilution. In any case, the net effect is still one of enhancement by an equimolar mixture of polynucleotides which gives a final GC concentration of 50 mol%. In contrast, DNA from

Escherichia coli which contains 52 mol% GC quenches quinacrine fluorescence, as does DNA from *Clostridium perfringens* with 32 mol% GC.

These observations suggest that the degree of fluorescence enhancement is not strictly a function of the AT/GC ratio but that the degree of interspersed of GC base pairs among AT base pairs plays an important role. Thus, in a comparison of two polynucleotides with the same base composition, the one which has a higher degree of GC base pair interspersed would be expected to show a greater degree of quenching. A corollary would be: for two polynucleotides with different base compositions, the polynucleotide with less GC could actually quench more if the GC base pairs were more evenly interspersed (compare *C. perfringens* DNA and $(dA)_n \cdot (dT)_n + (dG)_n \cdot (dC)_n$). An extreme example of GC interspersed would be one in which GC (and therefore AT) base pairs were distributed evenly throughout the length of the polynucleotide. Such DNA would be highly repetitive, a well known property of the DNA found at the centric regions of mouse chromosomes.

Caspersson and Zech⁵ originally proposed that preferential binding to accessible sites is the determinant of quinacrine fluorescence. In a recent work⁵ the possibility of quinacrine fluorescence enhancement by AT-groups and quenching by GC groups is acknowledged. On the other hand, our fluorometric studies of dyes that bind to DNA lead us to the conclusion that for those dyes which have useful fluorescence staining properties for chromosomes, the fundamental determinants of the fluorescence pattern seen are the bases and their relation to each other; both the primary and secondary structures can play a role. Whether the fluorometric properties of the dye are actually expressed may depend on secondary factors such as accessibility, controlled by unidentified hypothetical proteins. The results described here exemplify a further application of this principle.

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Cytosine Arabinoside and Rosette Formation in Mouse Retina

Glücksman and Tansley¹ reported that the developing retina was very vulnerable to X rays and this has been confirmed by many other investigators²⁻⁴. Some drugs which inhibit DNA synthesis may also inhibit cellular proliferation and thus cause maldevelopment of the retina. This would result because, in the neural retina of the suckling animals, active cellular proliferation is taking place producing neurones at the inner and outer nuclear layers^{5,6}.

Cytosine arabinoside, a common antitumour drug, inhibits DNA polymerase^{7,8}. Because of this, it is used in the treatment of some viral infections, such as herpesvirus infection⁹⁻¹¹ and cytomegalic inclusion disease¹². We have investigated the possible effects of this drug on the developing mouse retina.

One hundred and twenty-one suckling mice, ICR-JCL

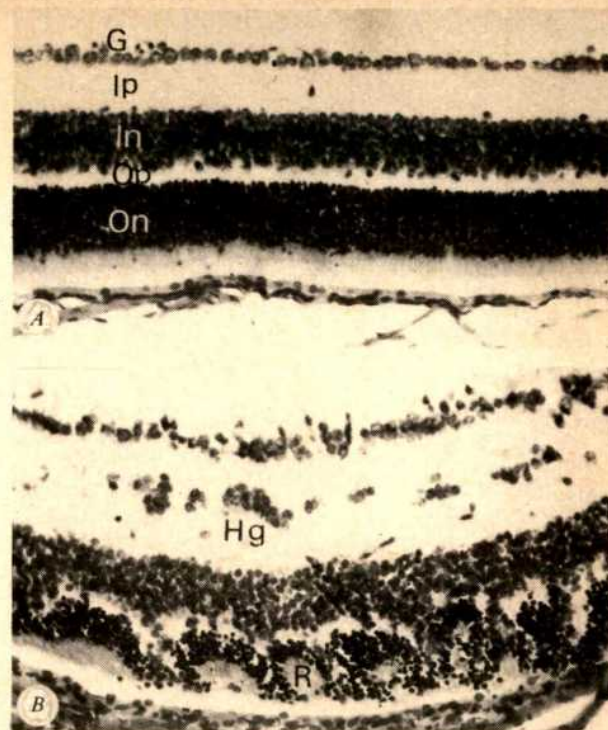


Fig. 1 A, Normal retina of 20-d-old mouse. G, Ganglion cell layer; Ip, inner plexiform layer; In, inner nuclear layer; Op, outer plexiform layer; On, outer nuclear layer. B, Retina of 20-d-old mouse which had three successive doses of (50 mg kg⁻¹) cytosine arabinoside on postnatal days 2, 3 and 4. R, Rosette; Hg, heterotopic ganglion cell in the inner plexiform layer.

strain, were divided into two groups. Forty-seven mice were injected subcutaneously with cytosine arabinoside (30 mg kg⁻¹) 2, 3 and 4 d after birth (group 1). Seventy-four animals were similarly treated with 50 mg kg⁻¹ (group 2). Treated animals of both groups were then killed 5, 7, 10, 15, 20 and 30 d after birth. The eyes were removed, fixed in either Bouin's or Carnoy's solution, embedded in 'Paraplast' and cut into 6 μ m sections. The sections were stained either with haematoxylin-eosin or 1% cresyl violet. Retinas of untreated mice of the same age were used as controls.

Twenty-four hours after the final injection of cytosine arabinoside the undifferentiated nuclear layer was seen to be selectively destroyed and to contain a large quantity of nuclear debris. Large cavities resulting from the necrosis of undifferentiated cells were also prevalent in this layer. In the retina of 5-d-old controls many large, round, pale nuclei, which later formed the inner nuclear layer, were seen at the inner zone of the undifferentiated nuclear layer. On the outer surface of this layer, however, mitosis was still common. When the experimental animals were examined on postnatal day 7, the nuclear debris and cavity in the nuclear layer had disappeared although many rosettes were found, either scattered or in rows, at the outer nuclear layer. A few cells in mitosis were found on the inner surface of this structure. By this time the retina of a 7 d old control was already similar to that of an adult. Even 20 and 30 d after birth, rosettes were found in 81 to 67% of the retinas in group 1 and in all of group 2 (Table 1). They were especially numerous on the portion of the retina close to the ora serrata. The ganglion cells of the treated mouse were arranged irregularly and the inner plexiform layer was approximately twice as wide as that of the controls. Within the inner plexiform layer, heterotopic cells, which are morphologically similar to ganglion cells, were found in clusters or in rows (Fig. 1).

Table 1 Incidence of Rosettes in the Retinae of Treated Mice

Group	No. of animals treated	Age when killed (d)												No. killed	No. killed	No. killed						
		5		7		10		15		20		30										
		No. killed	0 + + + + +	No. killed	0 + + + + +	No. killed	0 + + + + +	No. killed	0 + + + + +	No. killed	0 + + + + +	No. killed	0 + + + + +	No. killed	0 + + + + +	No. killed	0 + + + + +					
1	47	5	4	1	8	1	1	6	8	1	2	5	6	3	11	2	1	1	7	9	3	6
2	74	9	5	4	11	1	2	8	18	1	17	8	1	1	17	1	2	14	12	1	11	
Control	25	4	4		4	4			4	4		4	4		4	4			5	5		

The animals belonging to group 1 were given three successive doses of cytosine arabinoside (30 mg kg⁻¹). The animals in group 2 were given three successive doses of 50 mg kg⁻¹. +, One to four rosettes; ++, five to ten rosettes; + + +, more than ten rosettes.

The total effect on the retina caused by the administration of cytosine arabinoside to the suckling mouse is summarized in Table 1. Total doses used in this experiment are not very different from those used clinically for the treatment of leukaemia or viral infection. The results therefore indicate the possibility that such treatment may cause lasting damage to the developing retina.

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Modulation of Lymphocyte Receptor Redistribution by Concanavalin A, Anti-mitotic Agents and Alterations of pH

VARIOUS lymphocyte surface receptors can be redistributed after cross linkage by external ligands, leading to the formation of patches and caps¹. At 21° C and 37° C concanavalin A (con A) in concentrations greater than 5 µg ml⁻¹ inhibits patch and subsequent cap formation induced by anti-immunoglobulin and other reagents^{2,3}. Con A can also induce cap formation by its own receptors under certain conditions, notably after binding at 4° C^{3,4}. Thus con A has two antagonistic activities in modulating lymphocyte surface receptor distribution and their expression depends on the conditions of incubation. We now report results suggesting that colchicine-binding proteins⁵ (possibly those of the microtubules) are important in the modulation of cell surface mobility. In addition, we have found that alterations of pH affect the ability of lymphocytes to form patches and caps.

Splenic lymphocytes from NCS mice (Rockefeller University) were used. The preparation of fluorescein-labelled con A (fl-con A) has been described elsewhere². Unless otherwise noted, Hanks' balanced salt solution (HBSS) containing 5% (v/v) foetal bovine serum was the medium.

After lymphocytes had been incubated with 100 µg ml⁻¹ fl-anti-immunoglobulin at 37° C for 10 min, about 45% of the total cells were stained and 85% of them showed caps; however, if 100 µg ml⁻¹ con A was added before the fl-anti-immunoglobulin, 45% of cells were stained but only 1%

showed caps. If the cells were pretreated for 1 h at 37° C with 10^{-4} M colchicine, an anti-mitotic agent⁶ which dissociates microtubules⁵, 30% of those exposed to con A and fl-anti-immunoglobulin showed typical patch formation followed by cap formation. Because colchicine did not induce cap formation, it must have partially suppressed the inhibitory effect of con A on patch and cap formation with fl-anti-immunoglobulin (Fig. 1). Similarly, incubation with $100 \mu\text{g ml}^{-1}$ fl-con A at 37° C for 15 min showed that 95% of cells were stained, with only 1–2% showing caps, but 20% or more cap-forming cells were observed when cells were pretreated with 10^{-4} M colchicine.

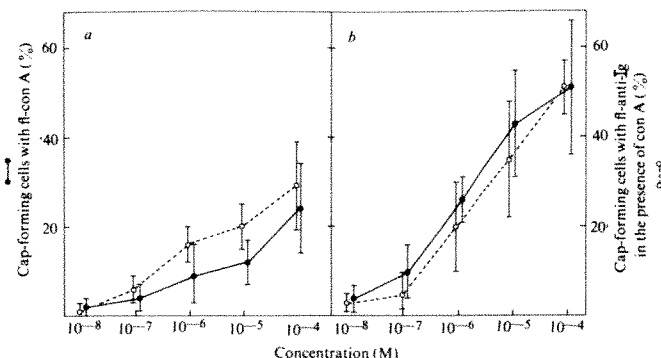


Fig. 1 Effect of colchicine (a) and vinblastine (b) on inhibition of patch and cap formation by con A. Cells were incubated separately with various concentrations of colchicine and vinblastine at 37° C for 30 min and incubated for another 10 min with $100 \mu\text{g ml}^{-1}$ fl-con A (●) or with $100 \mu\text{g ml}^{-1}$ fl-anti-immunoglobulin in the presence of $100 \mu\text{g ml}^{-1}$ con A (○). Cap formation was determined as described previously³.

Time of incubation with colchicine was not critical, for the drug affected cap formation with fl-con A even if both were added at the same time. Furthermore, when cells were incubated with fl-con A at 37° C for 15 min, washed, and then incubated at 37° C for 1 h in the presence of 10^{-4} M colchicine, 25% of cells formed caps. In contrast, if colchicine was omitted, only about 2% of cells showed caps.

Similar but more marked effects were observed using the *Vinca* alkaloid, vinblastine⁷ (Fig. 1). Other anti-mitotic agents including colcemid, vincristine⁷, and podophyllotoxin⁸ also suppressed the inhibitory effect of con A (Table 1). The relatively weak effect of podophyllotoxin may be related to its impurity as well as its limited solubility in the medium. Griseofulvin⁹ did

not influence the inhibition of patch and cap formation by con A; however, some commercial samples of griseofulvin are reported to lack anti-mitotic activity⁹. Although colchicine, vinblastine and strychnine affect erythrocyte membrane structure⁹, strychnine had no obvious effect in our system. Lumicolchicine¹⁰, a structural isomer of colchicine that does not bind to colchicine-binding proteins and is devoid of anti-mitotic activity, had no effect at concentrations comparable with those used with colchicine (Table 1).

To test the reversibility of the colchicine and vinblastine effects, cells were incubated with each drug at 37° C, washed, incubated for various times at 37° C and tested for cap formation (Fig. 2a). The effect of colchicine persisted for at least 2 h without significant decrease, and even after 6 h, 13% of cells had caps. The colchicine effect therefore seemed to be only partially reversible. In contrast, the vinblastine effect seemed to be almost fully reversible (Fig. 2a). The decrease in the number of cells forming caps with fl-con A after removal of vinblastine was not due to the intrinsic loss of ability to form caps, for there was no decrease in the number of cells forming caps with fl-anti-immunoglobulin during similar periods (Fig. 2b).

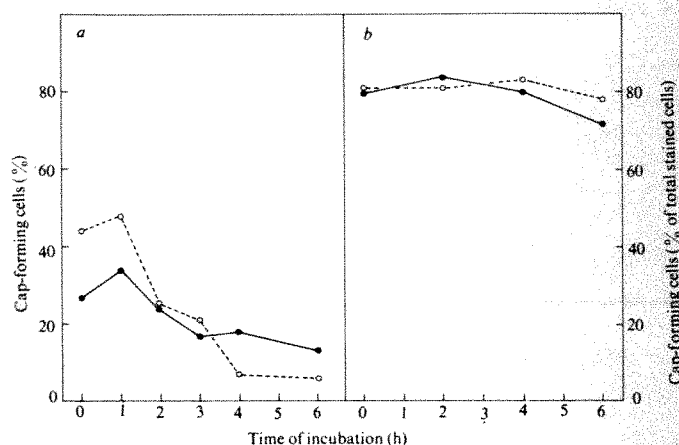


Fig. 2 Reversibility of colchicine and vinblastine effects. a, Cells were incubated separately with 10^{-4} M colchicine (●) and 10^{-4} M vinblastine (○) at 37° C for 30 min, washed twice and incubated at 37° C for various times in the medium containing no drug. The cells were subsequently incubated with a, $100 \mu\text{g ml}^{-1}$ fl-con A; b, $100 \mu\text{g ml}^{-1}$ fl-anti-immunoglobulin at 37° C for 10 min.

Table 1 Effect of Anti-mitotic Drugs on the Con A Effect

Drug	Concentration (M)	Caps (%) [*] with fl-con A [†]	Caps (%) [*] with fl-anti-immunoglobulin and con A [‡]
—	0	1 ± 1	1 ± 1
Colchicine	10^{-4}	24 ± 10	30 ± 8
Colcemid	10^{-4}	25	20
Vinblastine	10^{-4}	51 ± 12	51 ± 6
Vincristine	10^{-4}	19	15
Podophyllotoxin	10^{-3}	8	10
Lumicolchicine	5×10^{-4}	3	1
Griseofulvin	10^{-4}	1	2
Strychnine	10^{-3}	4	1

^{*} The percentage of the population showing cap formation was counted using samples of 100 cells or more. In cases where more than ten determinations were carried out, the values are given with standard deviations.

[†] $100 \mu\text{g ml}^{-1}$ fl-con A.

[‡] $100 \mu\text{g ml}^{-1}$ fl-anti-immunoglobulin and $100 \mu\text{g ml}^{-1}$ con A.

Low temperatures¹¹ and high hydrostatic pressures¹² dissociate microtubules. Although our efforts to demonstrate an effect of increased hydrostatic pressures yielded variable results, we found that low temperatures affect the number of cap-forming cells³. If splenic lymphocytes were incubated with $100 \mu\text{g ml}^{-1}$ fl-con A at 4° C, washed in the cold and then incubated at 37° C, approximately twenty times as many cap-forming cells were observed than after incubating cells at 37° C with $100 \mu\text{g ml}^{-1}$ con A. This cannot be explained by the fact that three times as many con A molecules are bound at 37° C than at 4° C, for the differences were observed even when identical numbers of molecules were bound at the two temperatures.

Our results suggest that the integrity of microtubular structures may be required for inhibition of patch formation by con A and that the mobility of cell receptors is modulated by structures associated with or related to microtubules. The concentrations of colchicine and vinblastine effective in our experiments are considerably greater, however, than those required to inhibit mitosis or disrupt microtubular structures visible by electron microscopy⁴. Moreover, microtubules with a diameter of 250 Å have never been observed either in or just under the cell membranes of lymphocytes. It is possible, therefore, that

the system affected by colchicine resembles the 250 Å microtubules but differs from them in organisation. Cationic alkaloids, such as vinblastine or strychnine, can precipitate with actin-like proteins isolated from various cells¹⁴. Although strychnine had no effect in our system, actin-like proteins may form structures that modulate the mobility of lymphocyte receptors. As colchicine, vinblastine, vincristine and podophyllotoxin bind to microtubules^{8,15} and because conditions that disrupt microtubules also affect the inhibition of patch formation by con A, a colchicine-binding protein resembling tubulin seems a more likely candidate than other proteins or phospholipids.

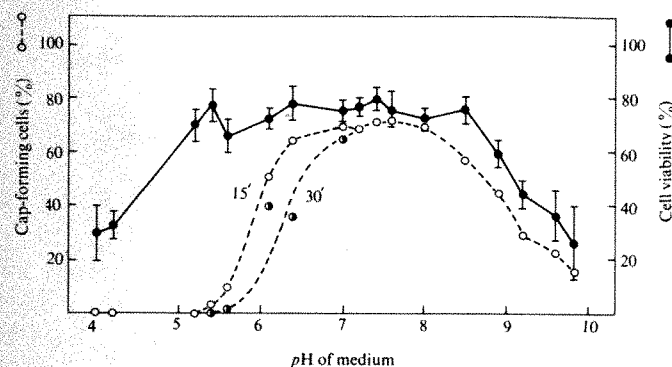


Fig. 3 Effect of pH on patch and cap formation. The following buffered isotonic media were used: 10 mM acetate-buffered saline (pH 4.2, 5.4), 10 mM citrate-phosphate-buffered saline (pH 4.0, 5.2, 5.6, 6.1, 6.4, 7.0), 10 mM Tris-HCl-buffered saline (pH 7.2, 7.6, 8.0, 8.4, 8.8), 10 mM glycine-NaOH-buffered saline (pH 8.5, 8.9, 9.2, 9.6, 9.8), PBS (pH 7.4), HBSS (pH 7.2). Cells were pre-incubated separately in those media at 37° C for 15 min and then incubated with fl-anti-immunoglobulin at 37° C for 10 min in the same media. Cell viability (●) was determined by the trypan blue dye exclusion; bars represent standard deviations of repeated measurements. Cap (○) formation was determined as described previously. The effect on cap formation with fl-anti-immunoglobulin is also shown after prolonged incubation (30 min) of cells in acidic media (●).

The observations reported here may be related to reports that colchicine affects both the agglutination induced by con A and phagocytic events in polymorphonuclear leukocytes^{16,17}, suggesting that the topographical distribution of con A receptors and transport sites for small molecules are controlled by microtubules. The differences we observed in reversibility of the effects of colchicine and vinblastine are similar to those obtained relative to the movement of mouse peripheral macrophages¹⁸.

So far only con A^{2,19}, other mitogenic lectins²⁰ and high concentrations of sugars¹⁹, such as 0.5 M D-mannose, have been shown unequivocally to affect patch formation reversibly. Loor *et al.*¹⁹ reported that LaCl₃ inhibits patch formation induced by anti-immunoglobulin. We could not repeat their experiments because we were unable to prepare 1–10 mM LaCl₃ solutions in media containing phosphate ions at neutral pH without precipitation or lowering of the pH of the medium. Moreover, 10 mM LaCl₃ in 10 mM Tris-HCl-buffered saline (pH 7.0) resulted in cell clumping with a drastic reduction in cell viability and precipitation of fl-anti-immunoglobulin.

We have found that cap formation induced by fl-anti-immunoglobulin was inhibited at both acidic and alkaline pH. A sharp decrease in the number of cap-forming cells was observed at pH 6.1 to 5.2 and neither patch nor cap formation was observed at pH 5.2. When cells were incubated for prolonged periods, the critical pH was more alkaline (Fig. 3). Because slight decreases in cell viability were observed within the effective range (Fig. 3) and the inhibition was reversible (Table 2), the decreases in cap-forming cells in acidic media cannot be accounted for by cell death. Patch formation was frequently observed in alkaline media even in cells not forming caps.

and the absence of caps paralleled the viability curve. It is likely, therefore, that the inhibition of cap formation in alkaline media is due to cell damage and to depression of cellular metabolism before cell death.

Table 2 Effects of Colchicine Treatment and Exposure to Low pH on Cap Formation

First incubation*	Second incubation†	Third incubation‡	I Caps (%) with fl-anti-immunoglobulin	II Caps (%) with fl-anti-immunoglobulin and con A	III Caps (%) with fl-con A
pH 7.2	pH 7.2	pH 7.2	77	2	3
pH 7.2	pH 5.2	pH 7.2	78	2	2
pH 7.2+ colchicine	pH 7.2	pH 7.2	81	39	31
pH 7.2+ colchicine	pH 5.2	pH 7.2	81	41	46

* Cells were incubated at 37° C for 30 min with or without 10⁻⁴ M colchicine and washed.

† Cells were incubated at 37° C for 15 min in citrate-phosphate-buffered saline (pH 5.2).

‡ Cells were incubated at 37° C for 10 min with 100 µg ml⁻¹ fl-anti-immunoglobulin in the absence (column I) or presence (column II) of 100 µg ml⁻¹ con A, or with 100 µg ml⁻¹ fl-con A (column III).

Unlike the inhibition by con A, the effect of acidic pH was not reversed even partially by colchicine. For example, when lymphocytes were treated with 10⁻⁴ M colchicine and subsequently incubated with fl-anti-immunoglobulin in medium at pH 5.2, cap-forming cells were not observed. The lack of effect of colchicine at pH 5.2 cannot be due to the release of molecules from colchicine-binding proteins¹⁵, because the effect was obvious if cells treated with colchicine and then washed were briefly incubated at pH 5.2, and returned to neutral pH (Table 2). The specific mechanism and sites of action mediating the inhibitory effect at acidic pH seemed to be different from those of con A. Patch formation is independent of metabolism^{1,2} and therefore the effects of acidic pH are not attributable to any effects of pH on metabolism. Acidic pH may affect phospholipid head groups of the membrane, the phase separation characteristics of the membrane lipids, or submembranous structures.

Our present and previous data^{20,21} suggest that both the tetravalence of con A and the integrity of a colchicine-binding structure are required for inhibition of patch formation. It is not yet clear whether con A can inhibit micropatch formation demonstrable at the electron microscopic level²² but not at the level of fluorescence microscopy. In any event, our results suggest that although cell receptors may be mobile in the membrane^{23,24} their relative mobility may be modulated by structures the exact nature of which remains to be defined. This hypothesis is compatible with observations²⁵ suggesting that some of the receptors on the cell surface penetrate the membrane possibly to interact with other cellular components.

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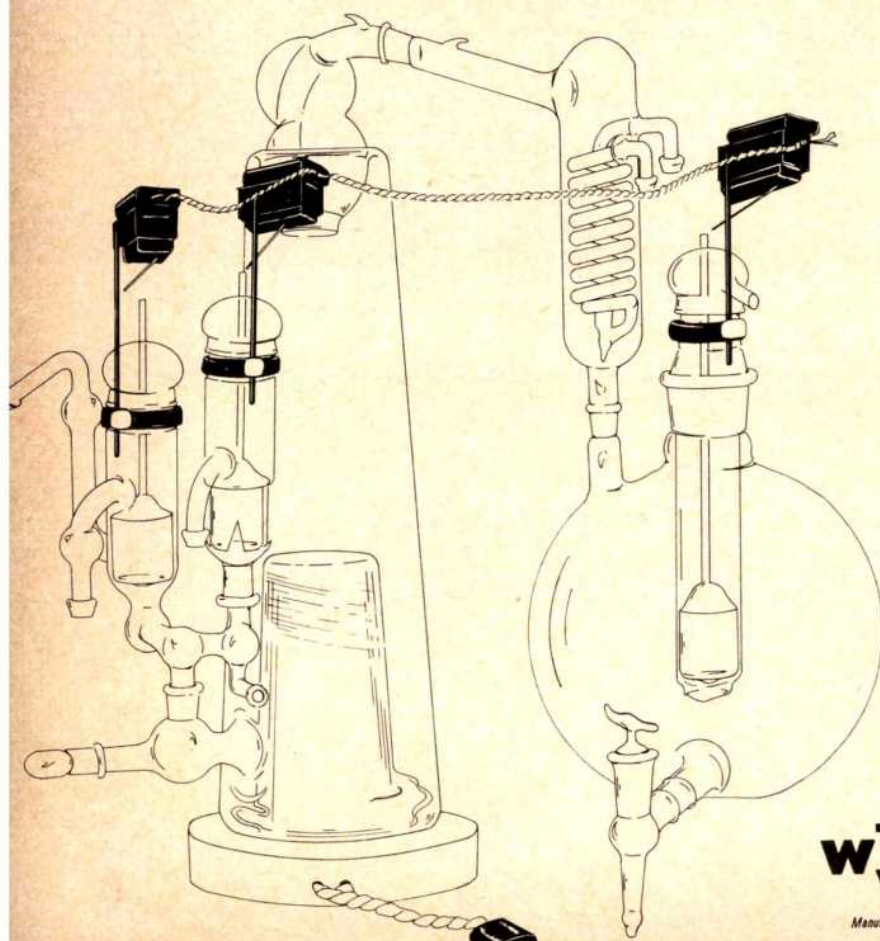
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Crossbands of *Caulobacter crescentus* Stalks serve as Indicators of Cell Age

BACTERIA in the genus *Caulobacter* have a life cycle with two distinct cell types¹: a non-motile mother cell with a stalk extending from one cell pole, and a polarly flagellated swarmer cell which has no stalk. During the life cycle the mother cell elongates and divides to produce a swarmer at its non-stalked pole. The swarmer forms a holdfast at the base of its flagellum and, before division, produces a stalk from the same site. The synthesis of the stalk occurs at the cell-stalk junction².

Structures variously called Querbalken, crossbands, and annuli have been reported in *Caulobacter* stalks since they were first observed in the electron microscope³⁻⁶. This study was undertaken to determine how the formation of these structures is related to the life cycle of the bacterium.

Caulobacter crescentus strain CB2-L was used in all experiments. It was maintained on medium MMB⁷.

In one series of experiments synchronous cultures were initiated with swimmers. *C. crescentus* was inoculated into a sterile, 500 ml, pear-shaped separatory funnel containing MMB and 400 g of 4 mm glass beads. The culture was incubated at room temperature for 24-48 h before the synchrony experiments were begun. Then approximately 4 l of sterile MMB was washed over the beads to remove all unattached or loosely attached cells. The flow was stopped for 15 min to allow swarmer cells to be released by mother cells attached to the beads. Then 150 ml was eluted from the column into a sterile 500 ml Erlenmeyer flask that was transferred to a shaker water bath at 30° C. Ten millilitre samples were collected and fixed with Lugol's iodine at zero time and at 30 min intervals thereafter for examination with the electron microscope (AEI EM6B at 60 kV). Enlarged prints of electron micrographs were used to measure stalk length, cell length, and number of crossbands. Total counts were determined on samples every 15 min using a Petroff-Hauser counting chamber. The curve shown in Fig. 1 was obtained.

The initial population consisted of 5.9×10^6 cells per ml. Oil immersion phase and electron microscopic counts indicated that the swimmers, C_0 , comprised about 90% of the total population (91.5 and 92.5%, respectively). At 30 min some cells

had begun to synthesise stalks but the average stalk length was only 0.10 μ m. At 1 h stalk synthesis had commenced in almost all cells, and the average stalk length was 0.5 μ m. Only one stalked cell in fifty contained a crossband. By 1.5 h the range of stalk lengths was 0.55-1.40 μ m with an average of 1 μ m. About 47% of the stalked cells (twenty-two out of forty-seven) had one crossband (only one in fifty had more). Although many of the cells at 1.5 h had indentations indicating they were in the process of division, most cells separated in the succeeding half hour.

At 2 h, the average stalk length decreased to 0.9 μ m because newly formed swimmers of the next generation, C_1 , had begun to produce stalks. If it is assumed that all C_0 cells had stalks longer than 0.55 μ m (the minimum length observed in these cells at 1.5 h), then 69% (forty out of fifty-eight) had one stalk septation and the average stalk length was 1 μ m, or about the same as at 1.5 h. Therefore the rate of stalk synthesis approached zero at the time of cell division and cell separation.

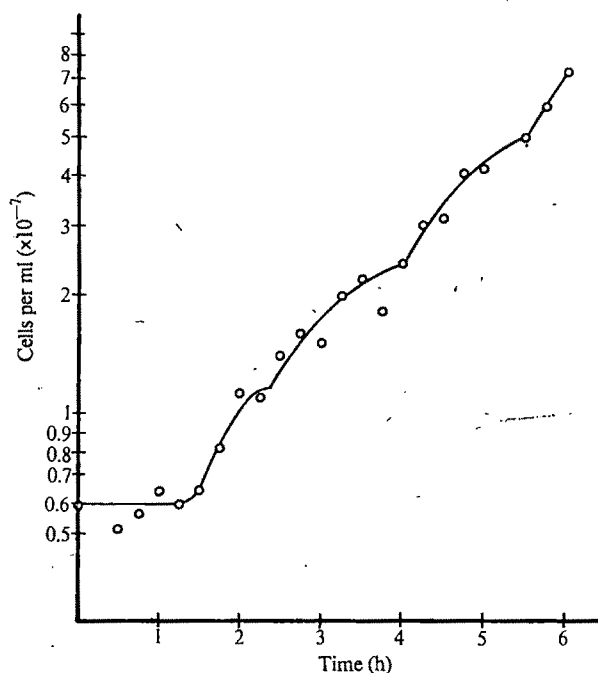


Fig. 1 Growth of a synchronous culture of *Caulobacter crescentus* CB2-L initiated with swarmer cells. Cells began dividing at about 1.5 h and had completed division by about 2 h. The second doubling was completed by 4 h and the third by 5.5 h.

At 2.5 h stalks of the C_0 population had resumed elongation and the average length was 1.25 μ m. Assuming that the minimum stalk length of these cells increased at the average rate of elongation it would be 0.8 μ m at 2.5 h: 88% of the cells with stalks that length or longer, which are presumably the C_0 population, had a single crossband. Thus, most, if not all, cells of this strain produce a crossband during or shortly after cell division. This conclusion is consistent with the independent studies of Jones and Schmidt⁸.

At 4 h, when the second doubling was completed, nineteen stalked cells had two crossbands and twenty-two had one. This is close to the 1:1 ratio expected if all C_0 cells had developed a second crossband and all C_1 cells had developed their first crossband following division. None of the fifty-two stalked cells examined had more than two crossbands at this time. At 5.5 h, when cell numbers had again doubled, cells with three crossbands were found. By this time, however, the synchrony had deteriorated considerably.

Stalk elongation continued after the first generation so that at 4 h the C_0 cells (those with two crossbands) had an average

stalk length of 1.65 μm and at 5.5 h the average stalk length of the C_0 cells, which now had 3 septa, was 1.75 μm . Apparently, during logarithmic growth, the average rate of stalk synthesis remains high for the first two generations and then decreases. We also noted that stalks with two and three crossbands were much longer (3.15 and 4.91 μm , respectively) during stationary phase than during logarithmic growth, presumably due to the effect of phosphorus limitation known to result in abnormally long stalks in *Caulobacter*².

The following picture of stalk and crossband formation best fits the above data: (1) swarmer cells may begin stalk synthesis any time after division (at one extreme we have an occasional cell undergoing separation having stalks at both exposed ends and, at the other extreme, rare cells dividing without stalks), (2) the rate of stalk synthesis decreases at the time of cell division, (3) crossband formation occurs during division, and (4) stalk elongation resumes after division.

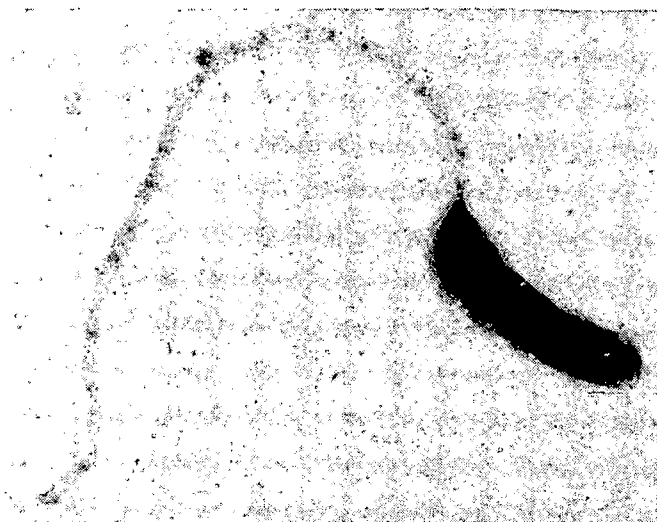


Fig. 2 A *C. crescentus* cell containing eighteen crossbands in its stalk. Most, or perhaps all, cells of this strain form a crossband in their stalks at the time of division so that the minimum age of the cell is eighteen generations.

Using another experimental approach a population of swimmers was grown in conditions of unlimited growth to determine whether crossbands were formed each generation even after numerous divisions had occurred. To accomplish this, swimmers from a logarithmic population were allowed 20–30 min to attach to a short section of sterile glass tubing. The tubing was then aseptically transferred to a siphon connected to a 20 l reservoir of sterile MMB (all at 30° C). The medium was passed through the chamber at a rate of about 40 ml h⁻¹ to remove newly formed swimmers. The section of tubing was removed after 52 h. The cells were fixed and gently dislodged from the wall of the tubing with a transfer loop and observed with the electron microscope. The estimated generation time was 2.7 h. Thus, the predicted maximum age of a cell was nineteen generations. If crossbands were formed each generation, then some cells would be expected to have nineteen crossbands. The maximum number of crossbands found was eighteen, close to the theoretical expectation (Fig. 2).

The results of this study indicate that the stalk of *C. crescentus* CB2-L continues to elongate beyond the first generation and crossbands are formed in most, if not all, cells during the time of division. It seems likely that all caulobacters which produce crossbands (all species in the genera *Caulobacter* and *Asticacaulis*) would produce them in the same manner, so that counting stalk crossbands may become a generally useful procedure for determining cell ages of bacteria in these genera. If so, the effect of cell age upon metabolism and other aspects of cell physiology can be investigated in this group of aquatic bacteria. In addition, it should be possible to follow the ageing of *Caulobacter* communities in their natural habitats.

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Histamine H₁ and H₂-Receptors at a Ganglionic Synapse

MANY humoral agents are capable of modulating synaptic transmission in sympathetic ganglia and it has been proposed that a variety of receptors are present at the ganglionic synapse (see Haefely¹). There are thus many possible modulatory mechanisms at this synapse, some of which have a dual nature, the same substance being able both to facilitate and to depress ganglionic transmission by an action on two different populations of receptors. We wish to present evidence that histamine, like the catecholamines² and 5-hydroxytryptamine (serotonin)³, has a dual action at the ganglionic synapse.

Trendelenburg^{4,5} demonstrated that histamine can facilitate transmission through the feline superior cervical ganglion *in vivo* and found that this facilitation could be prevented by the classic anti-histaminic drug, mepyramine⁶. We have observed that histamine can either depress or facilitate transmission in the rabbit superior cervical ganglion depending on circumstances. A dual action of histamine on blood pressure has been reported⁶ and it has been proposed that the pressor effects are due to activation of one type of histamine receptor, the H₁-receptor, while the depressor effects are due to activation of a second type of receptor, the H₂-receptor (J. W. Black, D. A. A. Owen, and E. M. Parsons, unpublished). Whereas H₁-receptors are blocked specifically by mepyramine, H₂-receptors are unaffected by this drug but may be blocked by burimamide (N-methyl-N-(4-(5-imidazolyl)butyl)thiourea)⁷. We wished to establish whether H₁- and H₂-receptors were present at the ganglionic synapse and whether they were responsible for the observed dual actions of histamine.

The action of histamine was investigated on the rabbit isolated superior cervical ganglion in a bath allowing continuous superfusion of the ganglion with Krebs solution at 37° C⁸. Drugs were added to the superfusate either so as to give a constant concentration or by injection of a fixed amount into the superfusion stream. Injections into the superfusion stream are dispersed in a volume of about 10 ml. Stimuli, either submaximal or maximal for eliciting the initial (Sa) component of the postganglionic compound action potential, were delivered to the preganglionic nerve trunk about 30 mm proximal to the ganglion. Postganglionic action potentials were recorded from the internal carotid nerve at least 3 mm distal to the ganglion. Sa amplitude was measured from the pre-existing baseline; in none of the experiments reported here was subdivision of the

Sa component observed. Facilitation or depression is presented in the text as a percentage of estimated control values, allowing for any progressive change in control values with time.

The postganglionic compound action potential evoked by a single stimulus (response elicited at 30 s or, more usually, 1 min intervals) was reduced in amplitude in twelve out of thirteen preparations by histamine acid phosphate given as a constant superfusion ($0.33\text{--}33\text{ }\mu\text{M}$) or by injection of $0.1\text{--}0.33\text{ }\mu\text{mol}$ into the superfusion stream; in only one preparation was the response facilitated by histamine. The mean reduction of responses to maximal stimuli by $3.3\text{ }\mu\text{M}$ histamine ($1\text{ }\mu\text{g ml}^{-1}$) was $14\% \pm 3\%$, $n=8$. The effect of similar concentrations of histamine on action potentials evoked by continuous repetitive stimulation at 2 Hz was less consistent. Repetitive stimulation at this frequency itself induces a substantial facilitation of responses to both submaximal and maximal stimuli as a result of intrinsic modulatory processes⁸; thus, responses to maximal stimuli in these experiments were facilitated by $30\% \pm 3\%$, $n \pm 5$. In contrast to its effect on single responses, histamine depressed the responses to repetitive (2 Hz) stimulation in only one of eleven preparations; in six preparations histamine had no unequivocal effect, while in four preparations a facilitation was observed. In one experiment, $33\text{ }\mu\text{M}$ histamine caused a 29% reduction of responses to single submaximal stimuli (Fig. 1a) and in the same preparation caused a transient 19% facilitation of the responses elicited by stimulation at a frequency of 2 Hz (Fig. 1b).

It seems possible that the facilitatory effect of histamine, sometimes seen when repetitive stimulation was employed, may reflect an action of the drug often masked by its depressant action. Our results suggest that the depressant actions are usually predominant when responses are evoked by single stimuli; with repetitive stimulation, perhaps as a consequence of the activation of intrinsic facilitatory processes, the depressant actions of histamine are less apparent. Mepyramine, the classical antagonist of histamine H_1 -receptors, did not antagonise the histamine-induced depression of responses to single stimuli. On the contrary, in two experiments the depression produced by $3.3\text{ }\mu\text{M}$ histamine was increased in the presence of $2.5\text{ }\mu\text{M}$ mepyramine maleate ($1\text{ }\mu\text{g ml}^{-1}$). In Fig. 2 the histamine-induced depression was increased from 16% to 38% in the presence of mepyramine. In the only experiment in which histamine facilitated responses to single stimuli, the 3–12% facilitation induced by $3.3\text{ }\mu\text{M}$ histamine was replaced by a 22% depression in the presence of mepyramine. On the assumption that the increased depression is due to antagonism by mepyramine of a concomitant facilitatory action of histamine mediated by H_1 -receptors, the characteristics of the depressant action of histamine are best studied in the presence of mepyramine. Other experiments suggested that $2.5\text{ }\mu\text{M}$ mepyramine was adequate for suppression of the facilitatory effects induced by $3.3\text{ }\mu\text{M}$ histamine. In preparations exposed continuously to $2.5\text{ }\mu\text{M}$ mepyramine, the histamine-induced depression of the evoked response was dependent on concentration and the threshold concentration was around $0.03\text{ }\mu\text{M}$. The mean reduction of responses to single stimuli by $3.3\text{ }\mu\text{M}$ histamine in the presence of mepyramine was $25 \pm 6\%$, $n=4$.

If the histamine-induced depression is mediated by H_2 -receptors, this action should be antagonised by the H_2 -receptor antagonist, burimamide. We chose concentrations of burimamide which have been shown to cause significant blockade of H_2 -receptors in the vascular system of the rabbit and on guinea pig isolated atria⁷. In Fig. 2, it can be seen that addition of $4.7\text{ }\mu\text{M}$ burimamide ($1\text{ }\mu\text{g ml}^{-1}$) increased the rate at which recovery from the histamine-induced depression occurred after removal of histamine from the superfusion medium. Further, a subsequent superfusion with $3.3\text{ }\mu\text{M}$ histamine in the presence of both mepyramine and burimamide ($4.7\text{ }\mu\text{M}$) caused a much smaller depression (17%) of the evoked response; increasing the burimamide concentration to $47\text{ }\mu\text{M}$ almost abolished the depressant action of histamine in this experiment. In three out of five experiments, a combination of $2.5\text{ }\mu\text{M}$ mepyramine and

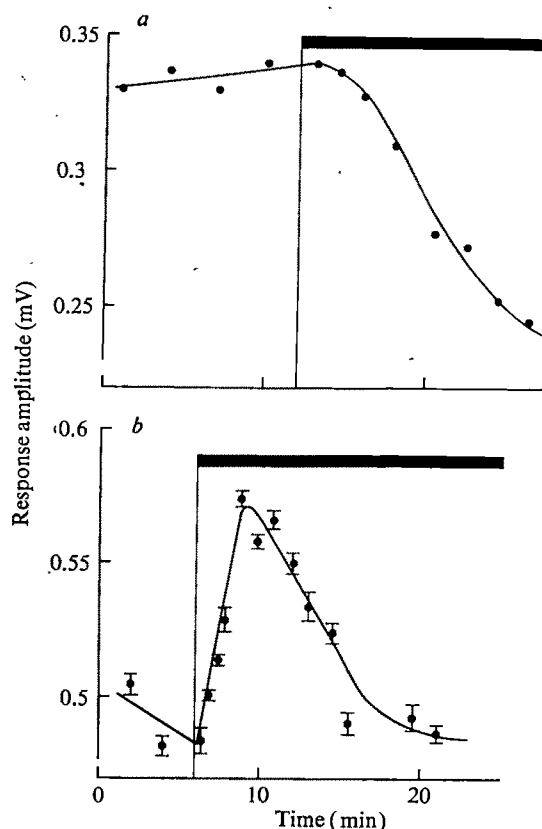


Fig. 1 Effect of histamine on amplitude of postganglionic compound action potential evoked by a single submaximal stimulus (a) or by repetitive submaximal stimulation at 2 Hz (b). Histamine ($33\text{ }\mu\text{M}$) present in perfusion medium for periods indicated by the black bars. In (a) each point represents a single observation or the mean of two or three observations. In (b) each point is the mean $\pm$ s.e.m.

$47\text{ }\mu\text{M}$ burimamide completely abolished the effects of $3.3\text{ }\mu\text{M}$ histamine on responses to single stimuli; in the other two preparations a residual histamine-induced depression of about 3% remained. The presence of both blockers also completely abolished the actions of $0.1\text{ }\mu\text{mol}$ ($30\text{ }\mu\text{g}$) histamine injections into the superfusion stream.

In the absence of mepyramine, $47\text{ }\mu\text{M}$ burimamide consistently antagonised the depressant action of histamine and revealed the facilitatory action. In the experiment shown in Fig. 3, $3.3\text{ }\mu\text{M}$ histamine induced a 16% depression of the evoked response on initial superfusion and a 17% depression on a second superfusion. Burimamide ($47\text{ }\mu\text{M}$) accelerated the recovery from this second histamine-induced depression, and a third exposure to histamine in the presence of burimamide resulted in a 10% facilitation of the evoked response. The subsequent addition of $2.5\text{ }\mu\text{M}$ mepyramine to the superfusion medium completely abolished this facilitation, only a small depressant action being apparent on a fourth superfusion with histamine. In each of four experiments superfusion with $3.3\text{ }\mu\text{M}$ histamine in the presence of burimamide produced a facilitation ($10\% \pm 1\%$).

If the lack of effect of histamine on many preparations stimulated at 2 Hz is due to approximately equal facilitatory H_1 - and depressant H_2 -actions, then blockade of one type of receptor should reveal the action mediated by the other. This was the case: one preparation, which initially failed to respond to injections of $0.1\text{ }\mu\text{mol}$ histamine, responded with 7–8% facilitation of the evoked action potentials in the presence of $47\text{ }\mu\text{M}$ burimamide; in another preparation, $2.5\text{ }\mu\text{M}$ mepyramine revealed a small (4–5%) histamine-induced depression to injections of $0.1\text{ }\mu\text{mol}$.

Neither mepyramine nor burimamide in the concentrations studied here had any detectable effect by themselves on the

amplitude of the postganglionic compound action potential. In some experiments (see, for example, Fig. 3), long-term fluctuations in action potential amplitude occurred, but these appeared to be unrelated to the addition of drugs.

On the assumption that mepyramine and burimamide are relatively specific antagonists of H_1 - and H_2 -histamine receptors⁷ respectively, the above results are consistent with the presence at the ganglionic synapse of both these receptor types, H_1 -receptors mediating the facilitatory actions of histamine and H_2 -receptors mediating the depressant actions. It is interesting that a recent report⁸ has suggested that there are two sorts of 5-hydroxytryptamine receptors at the ganglionic synapse, one mediating a depressant, the other an excitatory action. The localisation of the histamine receptors either presynaptically or postsynaptically is not possible on the available evidence, although it is known that histamine causes little or no measurable depolarisation of ganglion cells (ref. 1; and D. I. Wallis and B. Woodward, unpublished). The presence at the ganglionic synapse not only of H_1 - and H_2 -histamine receptors, but also of α and β adrenoreceptors², muscarinic acetylcholine receptors, tryptamine receptors^{3,9}, γ -aminobutyric acid receptors^{10,11}, and receptors to certain polypeptides¹ is extremely puzzling. Are all these receptors merely vestigial? Do they perhaps represent an inevitable but physiologically insignificant sensitivity of the mechanisms operating at the synapse to biologically active substances or are they, on the other hand, involved in a complex

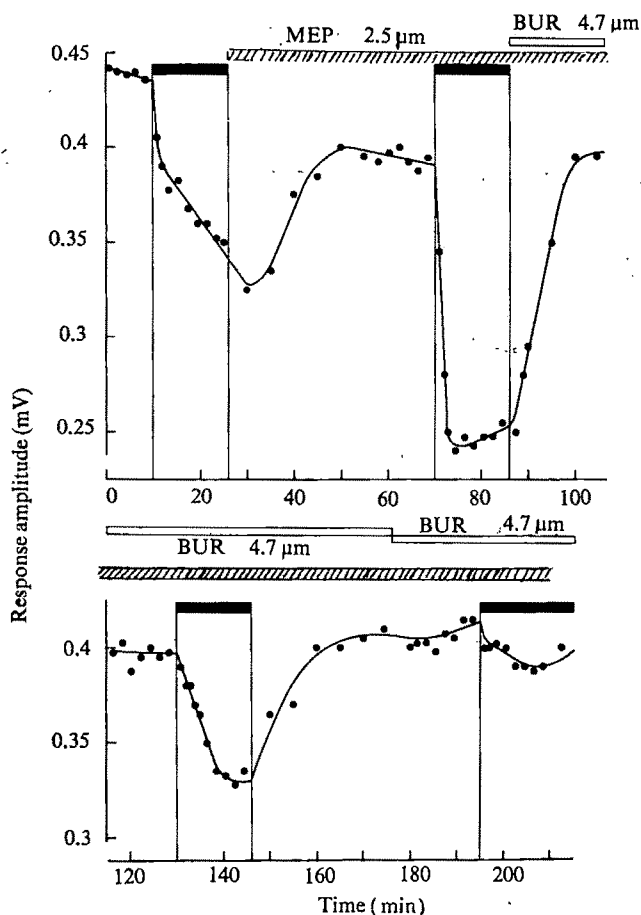


Fig. 2 The effects of mepyramine and of a combination of mepyramine and burimamide on the depressant action of histamine. Responses to single maximal stimuli. Histamine ($3.3 \mu\text{M}$) present in perfusion medium for periods indicated by the black bars. Each point represents a single observation or the mean of two observations. Mepyramine (MEP) ($2.5 \mu\text{M}$) present for the duration of the hatched bar and during the third and fourth exposures to histamine. Burimamide present during the periods indicated by the white bars, initially as a $4.7 \mu\text{M}$ solution (BUR $4.7 \mu\text{M}$) and subsequently as a $47 \mu\text{M}$ solution (BUR $47 \mu\text{M}$).

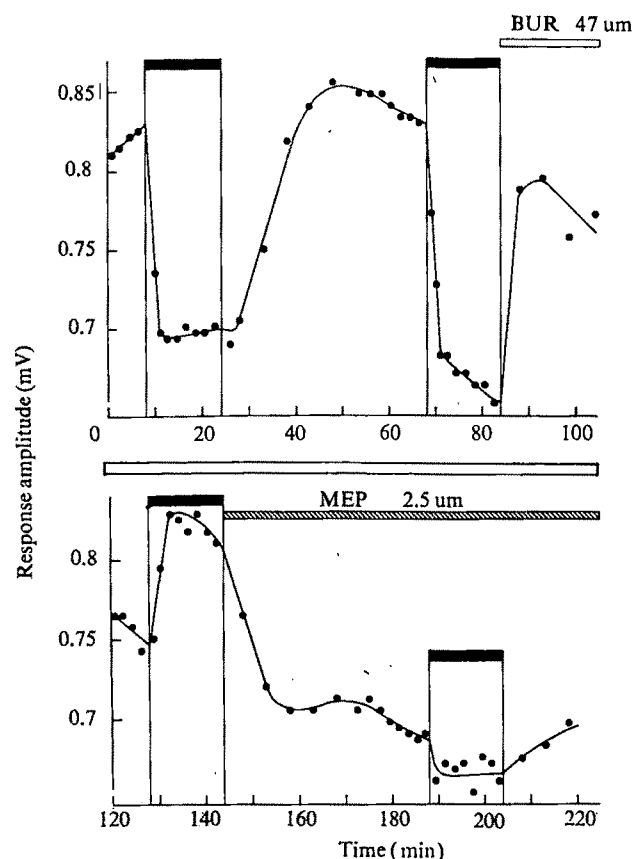


Fig. 3 The effects of burimamide and of a combination of burimamide and mepyramine on the action of histamine. Responses to single maximal stimuli. $3.3 \mu\text{M}$ histamine present in perfusion medium for periods indicated by the black bars. Each point represents a single observation or the mean of two observations. $47 \mu\text{M}$ burimamide (BUR) present for the duration of the white bar and during the third and fourth exposures to histamine. $2.5 \mu\text{M}$ mepyramine (MEP) present during the period indicated by the hatched bar.

system of regulation by which agents carried in the blood stream or released locally can exert an important influence over the transmission process?

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Role of Insulin as a 'Permissive' Hormone in Mammary Gland Development

THE growth and differentiation of the mammary gland is controlled by the synergistic action of insulin, prolactin and ovarian or corticosteroid hormones¹⁻⁴. The ovarian steroid induced alveolar development of the virgin mammary gland *in vivo* is mediated by activation of nucleic acid and protein synthesis⁵⁻⁹ and mitosis⁸⁻⁹. On the other hand, numerous studies using organ cultures, mostly of fragments of mid-pregnant mammary gland, emphasised the role of insulin as the mitogenic hormone in mammary gland development¹⁰⁻¹². This variable nature of responsiveness of the mammary tissue to hormones *in vivo* and in organ culture has been discussed in recent reports^{13,14}. The proliferative mammary gland of pregnancy, mostly used in these organ culture studies¹⁰⁻¹², should contain a large proportion of cells in the division cycle at the time of excision; we considered that hormonal regulation of the fate of these dividing cells during incubation *in vitro* may influence the interpretation of the results obtained from the organ culture studies. In order to test this possibility, mid-pregnant mammary cells of Balb/c mice were labelled for 1 h with ³H-thymidine (³H-dT) *in vivo*, and the transit patterns of the labelled cells reaching mitosis were determined at different times in organ culture.

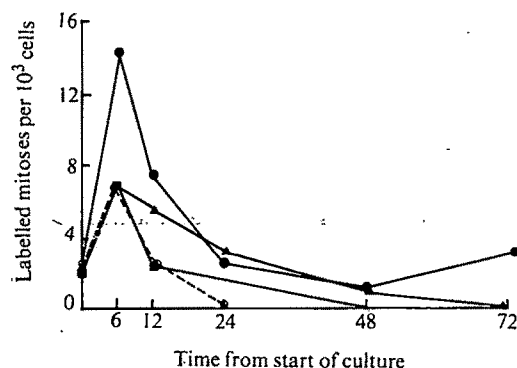


Fig. 1 Number of ³H-dT labelled mitoses per 1,000 mammary epithelial cells at different times in organ culture. The mammary gland of a 13-d-pregnant Balb/c mouse was used. Days of pregnancy were determined by the vaginal plug method. 100 μ Ci ³H-dT (49.2 Ci mmol⁻¹) (New England Nuclear Corporation, Boston, Mass.) was injected intraperitoneally 1 h before killing by cervical dislocation. Pulse labelling time of ³H-dT in mouse mammary gland *in vivo* is 30 min¹⁵. For organ culture, fragments (1-2 mm) of mammary gland were incubated at 37°C in 95% O₂ and 5% CO₂ atmosphere in plastic Petri dishes containing Waymouth (MB 752/1) medium with penicillin⁶. The organ culture medium was supplemented with 5 μ g ml⁻¹ each of insulin (▲), or insulin + prolactin (●), or prolactin (■) or was unsupplemented (○). The cultures were terminated at different times and the explants were fixed in acetic acid and ethanol (1:3 v/v) for liquid emulsion autoradiography (Kodak NTB 2)⁴. The autoradiograms of histological sections were scored under a 100 $\times$ oil immersion objective. The data represent typical values of 3-4 sets of cultures and at each time point 5,000 cells from 4-5 explants were scored. Metaphase to telophase cells were counted as mitosis.

As expected, mammary epithelial cells were initially labelled at a high frequency. The average number of silver grains per nucleus was reduced at different times of incubation, suggesting that the slight initial increase in the frequency of labelling is due to the mitotic division of some of the labelled cells rather than to continued incorporation of ³H-dT during incubation. Figure 1 shows that in I medium and in P containing insulin or prolactin alone the frequency of labelled mitoses increased modestly at 6 h, then decreased to zero, whereas in IP medium the frequency of labelled mitoses increased more than seven-fold at

6 h, decreased until 48 h, and rose again at 72 h. In NH medium, the frequency of labelled mitoses after an initial rise decreased to zero at 24 h; both in P and in NH medium extensive alveolar degeneration also occurred at this time. These results show that the mammary cells which were in the progenitor compartment *in vivo* can continue through the cell cycle reaching mitosis in organ culture. The variations in the frequency of labelled cells reaching mitosis in I, IP, or P medium at different times indicate, however, that the hormones greatly influence the cell transit time in organ culture.

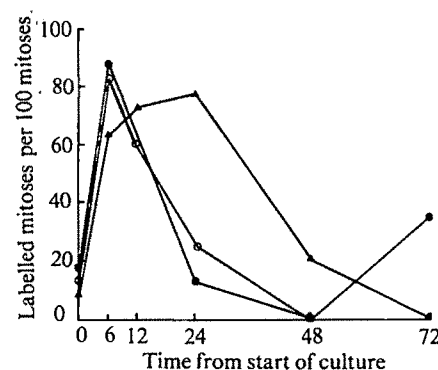


Fig. 2 Percentage of ³H-dT labelled mitoses among the mitotic cells. 100-200 cells were scored at each time point. ▲, Insulin; ○, prolactin; ●, insulin + prolactin. Other details as in Fig. 1.

In I medium the proportion of mitoses which are labelled increased slowly during the initial 24 h in organ culture, whereas in P and IP medium the proportion of labelled mitoses reached nearly 100% at 6 h, then dropped to zero at 48 h; in IP medium it rose again at 72 h (Fig. 2). The slow rate of increase of labelled mitoses between 6 h and 24 h in I medium strongly suggests that cells which were in the S phase *in vivo* spend a long time completing DNA synthesis *in vitro*, presumably because of a delayed recovery from the initial lag period in organ culture. The near 100% proportion of labelled mitoses at 6 h (7 h after injection of ³H-dT) in IP medium shows that mammary cells in IP medium complete DNA synthesis at a nearly normal rate (the duration of S in mid-pregnant mammary cells being 8-9 h (ref. 16)) reaching mitosis after a short initial latent period in organ culture. The unusually long S phase (20-21 h) (refs 15 and 16) of virgin mammary cells should similarly cause DNA synthesis to continue for an extended period during the recovery from the initial lag and this, rather than the earlier suggestion that virgin mammary cells acquire a delayed sensitivity to insulin in organ culture¹⁷, may be the explanation of the late rise of DNA synthesis in these cells in I medium.

Figure 3 shows that in I medium total mitosis slightly increased at 24 h but that it was below the initial value. In IP medium, a modest increase of mitosis at 6 h was followed by a two-fold rise at 12 h, a decrease to nearly zero at 48 h and another increase at 72 h. In P medium the general pattern was similar to that in I medium, but the mitotic activity was slightly higher than in the I medium until 24 h, and at 48 h it dropped to zero. In NH medium the cells failed to recover from the initial lag period and the mitotic activity declined to zero at 24 h. Since in I medium 65-75% of mitoses were labelled during the interval between 6 and 24 h (Fig. 2), the only slightly increased mitotic activity during this period indicates a negligible stimulation of new cells into mitosis by insulin in organ culture. In IP medium, since only 12% of mitoses were labelled at 24 h (Fig. 2), 88% of the cells in mitosis observed at this time must have been initiated into the division cycle during organ culture. Results in Fig. 3 further show that the addition of prolactin after 24 h incubation in insulin alone stimulated new cells into mitosis.

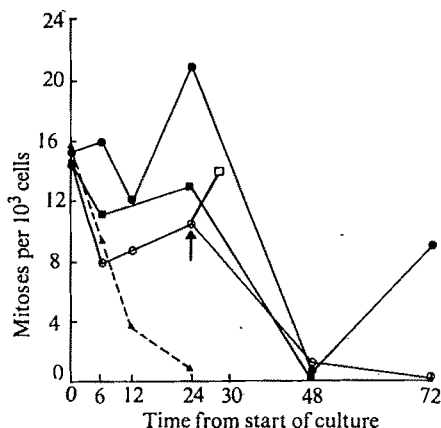


Fig. 3 Total mitotic (labelled and unlabelled) activity in mammary epithelium of mouse mammary gland in organ culture. ○, Insulin; ●, insulin + prolactin; ■, prolactin; ▲, no hormone; □, insulin 24 h, then insulin + prolactin up to 30 h. Arrow indicates the time prolactin was added. Other details are as in Fig. 1.

These observations thus show that under the conditions of the previous studies¹⁸⁻²⁰ mid-pregnant mammary cells which were in the division cycle *in vivo* should show increasing levels of ³H-dT incorporation (after 3-6 h pulse labelling *in vitro*) up to 24 h during their recovery from the lag period in I medium, which may lead to the interpretation that insulin alone stimulated DNA synthesis and mitosis in the mammary epithelial cells in organ culture^{11,12}. Our results suggest, however, that the cells which divide in the mammary tissue during the early hours of insulin-supplemented organ culture are mostly those which had already begun the division cycle in the mid-pregnant mammary gland *in vivo*. Insulin alone does not initiate new cells into proliferation, but acts as a 'permissive hormone'²¹ supporting completion of the division cycles of those cells which were initiated *in vivo*. The permissive action of insulin is, however, obligatory for the mitogenic action of prolactin in organ culture of mouse mammary tissue. Since exogenous ovarian steroids are detectable in the mammary tissue 72 h after a single injection²² the mitogenic action of insulin plus prolactin may be synergistic with the endogenous ovarian hormones carried in the mid-pregnant mammary tissue in organ culture. Contrary to earlier suggestions^{11,12} the requirement of hormones for mouse mammary cell proliferation may not be different *in vivo* and in organ culture.

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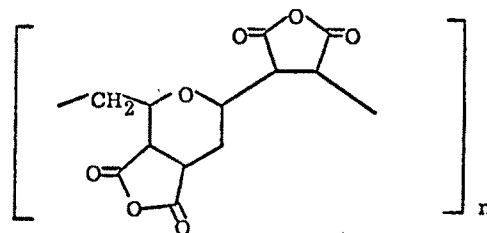
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Divinyl Ether-Maleic Anhydride (Pyran) Copolymer used to demonstrate the Effect of Molecular Weight on Biological Activity

DIVINYL ether and maleic anhydride form a 1:2 copolymer, which is reported to have the structure shown here¹. It is commonly known as pyran copolymer, although we prefer to call it DIVEMA, an acronym for divinyl ethermaleic anhydride. It has been designated as NSC 46015 by the National Cancer Institute.



The copolymer has various biological activities and has elicited considerable interest, as demonstrated by more than forty articles since 1967. DIVEMA has activity against several solid tumours, for example, adenocarcinoma 755², Lewis lung carcinoma³, C3H mouse mammary tumour³, and has been approved for initial clinical evaluation. It induces interferon⁴; it is active against several viruses, including Friend leukaemia^{5,6}, Rauscher leukaemia⁶, Moloney sarcoma⁷, vesicular stomatitis⁸, Mengo⁹, MM¹⁰ and foot-and-mouth disease¹¹; it has antibacterial¹² and antifungal activity^{12,13}; it stimulates immune response¹⁴⁻¹⁷; it inhibits adjuvant disease¹⁸, and it is an interesting anticoagulant¹⁹.

Several observations led us to a more thorough investigation of the structure of DIVEMA. Degraded material was found to have considerably lower acute toxicity in mice. Although most of a polymer prepared with ¹⁴C-labelled maleic anhydride was excreted by mice fairly rapidly, a portion was excreted very slowly²⁰. Munson *et al.*²¹ had shown a biphasic response of the reticuloendothelial system (RES) towards DIVEMA; initially there was a decrease in the rate of phagocytosis, followed by a considerable increase over the control after several days. Combining these observations, we hypothesised that the copolymer might consist of two materials, one toxic, very slowly metabolised, and responsible for the RES depression, and the other less

toxic, rapidly metabolised, and responsible for the RES stimulation. We assumed that the two materials would differ only in molecular weight, and that the high molecular weight portion was the undesirable material. This has now been confirmed.

To characterise the polymers, they were converted into their methyl esters by first refluxing them in methanol and then treating them with ethereal diazomethane. These esters were fractionated by gel permeation chromatography (GPC) on a Styragel column using tetrahydrofuran (THF) as solvent (similar results have been reported by Butler and Wu²⁰). A comparison of the molecular weights of the anhydride and the methyl ester demonstrated that no appreciable degradation had occurred during esterification. The intrinsic viscosities and weight-average molecular weights of fractions from a preparative GPC were determined in THF. They were then analysed on an analytical GPC column and compared with known polystyrene standards on the same column using the same solvent. A plot of the peak-elution volumes against $\bar{M}_w[\eta]$ gave a single curve (Fig. 1), $\bar{M}_w[\eta]$ being the 'universal parameter'²³. We were then able to determine the molecular weights and the polydispersities of other samples by using this calibration curve. This procedure demonstrated that the usual slurry polymerisation to high conversion²⁴ leads to polymer with broad molecular weight distribution.

Our goal was the synthesis of polymers in the desired molecular weight range with a narrow distribution, since we felt that the high molecular weight portion which would be present if the distribution were broad would contribute more to toxicity than to activity. In an attempt to obtain sufficient sample for evaluation, several large-scale fractionations of anhydride were carried out on sand columns, using a procedure developed originally for the fractionation of polyolefins²⁵. Because it was difficult to obtain enough material for evaluation by fractionation, we turned to direct polymerisation. By low-temperature photochemically initiated solution polymerisation in THF, a solvent for the copolymer at low but not high temperatures, narrow distribution copolymer could be prepared; molecular weight could be controlled to some extent by varying the monomer con-

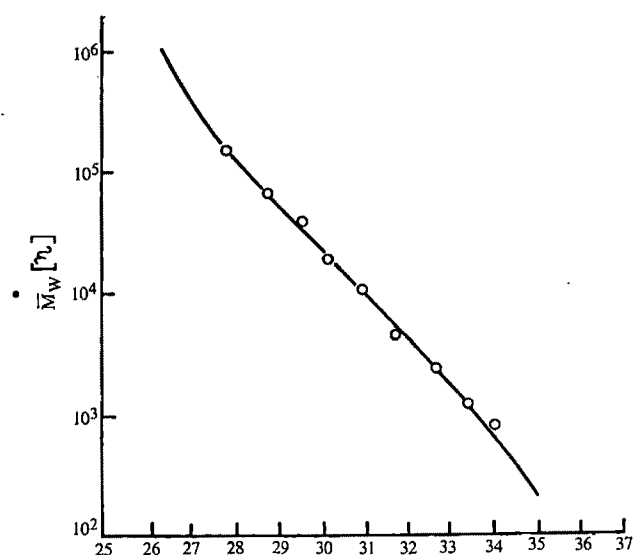


Fig. 1 Universal calibration curve for GPC using THF at 30°C. The line represents polystyrene standards, the circles pyran copolymer methyl ester fractions.

centrations. Acetone was a better solvent for the copolymer and almost any desired molecular weight could be obtained using a free-radical initiator in acetone with THF as a chain-transfer agent.

Table 1 lists different polymers in order of increasing molecular weight ($\bar{M}_p$ is the peak molecular weight from GPC of the methyl esters). NSC 46015 is a sample approved for clinical evaluation and XA 124-177 is a similar slurry polymer of higher molecular weight; both have broader molecular weight distributions than either the fractionated polymers or those made in solution. Even though the differences in acute toxicity are not large, it is apparent that

Table 1 Biological Activity of Various Samples of Pyran Copolymers

Sample	$\bar{M}_p^*$	$\bar{M}_w/\bar{M}_n^*$	Acute toxicity†	SGPT‡	Phagocytic index§	Endotoxin sensitisation¶ (% mortality)	Drug metabolism (% inhibition)	Antitumour Ehrlich†† (% inhibition)	Lewis lung‡‡ (T/C)
Control	—	—	—	30	0.044	0	—	—	—
A	2,500	1.7	—	34	0.105	0	—	66	> 130
B	3,000	1.7	—	48	0.073	0	15	—	> 171
C	3,900	2.3	—	30	—	0	—	—	> 133
D	5,200	1.9	—	54	—	20	—	—	125
E	6,900	1.9	127	46	0.055	0	0**	43	—
F	14,700	1.6	131	52	0.075	0	0	61	—
G	19,600	2.2	100	93	0.014	100	30**	45	—
H	25,000	2.6	—	132	—	100	—	—	—
I	44,800	2.3	87	96	0.010	100	57**	—	—
NSC 46015	22,500	3.7	96	> 200	0.021	100	67	67	> 117
XA 124-177	32,200	7.2	72	> 200	0.015	100	65	53	—

All tests except Lewis lung were done on white male Swiss NYLAR mice, polymer dose 25 mg kg⁻¹, given intravenously.

* From GPC of methyl ester.

† LD₅₀ intravenously.

‡ Serum glutamic pyruvate transaminase, Sigma Frankel Units.

§ From first order rate of carbon clearance, 24 h after injection.

¶ Endotoxin from *Salmonella typhosa*, 3 mg kg⁻¹ intravenous challenge.

|| Aminopyrine.

** Antipyrene.

†† Decrease in weight of tumour compared with control.

‡‡ Data obtained from Drug Research and Development, Chemotherapy, NCI; mean survival time, % of control.

toxicity as measured by the other criteria increased with increasing molecular weight. Thus, SGPT levels and inhibition of drug metabolism, both measures of liver function, increase with increasing polymer size, as does sensitisation to endotoxin. Phagocytosis is stimulated by low molecular weight polymer and depressed by high.

Most important, it was demonstrated that low molecular weight copolymers with narrow molecular weight distributions are not only low in toxicity but retain the antitumour activity shown by higher molecular weight samples against both Ehrlich adenocarcinoma and Lewis lung carcinoma in mice; the latter has proved extremely difficult to inhibit with standard chemotherapeutic agents^{26,27}.

Data available on the relationship between molecular weight and antiviral activity are limited to encephalomyocarditis in mice. The only conclusion which can be drawn at present is that with this virus a higher molecular weight is required for activity than for antitumour activity. Obviously other viruses must be examined before generalisations can be made.

In the light of the numerous literature references²⁸ to problems associated with the toxicity of pyran copolymer, the synthesis of materials with lower toxicity could be of major importance.

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Hyperthermia in Rabbits from Injection of Malaria Infected Erythrocytes in the Pre-optic Area

MALARIA, when introduced naturally by the bite of an anopheline mosquito, goes through an exoerythrocytic stage in the parenchymal cells of the liver. Here the malarial parasite matures to a mature merozoite that infects erythrocytes. When the parasite has multiplied, the red blood cell bursts and many new infective merozoites are released. These infect new erythrocytes. During lysis of erythrocytes the host develops a fever¹. It is not known whether the malarial parasite produces a pyrogen, like bacteria, or whether the malarial fever results from destruction of red blood cells.

The pre-optic area of the brain of mammals is thought to be the site of both temperature reception and integration in the central nervous system²⁻⁴. This area is far more sensitive to injected pyrogens than other sites in the brain⁵ suggesting that pyrogens interfere directly with nervous regulation of body temperature. Substantial fevers can be produced in mammals by injecting 1/100 of the effective intravenous dose of pyrogen directly into the pre-optic area⁶. Pyrogens released from leukocytes during infection are thought to be responsible for biogenic fevers, whereas pyrogens released from bacteria are scavenged from the blood and do not reach central nervous sites of temperature regulation⁶. When injected directly into the brain both classes of pyrogens induce fever, but leukocytic pyrogen acts more quickly (8 min) than bacterial pyrogens (45 to 60 min)^{4,5}. We took advantage of this differential sensitivity to test the pyrogenicity and nature of malarial parasites.

Rabbits, anaesthetized with chlorpromazine (25 mg kg⁻¹) followed by sodium pentobarbital (20 mg kg⁻¹), were implanted with cannulae (David Kopf) consisting of a twenty-two gauge needle mounted on stainless steel tube 4 mm in diameter with threads cut on outside and inside. The inside holds a set screw to retain a neoprene seal. The threads on the outside enable the cannula to be screwed directly to the skull. The cannula was further secured by acrylic powder mixed with methylmethacrylate solvent. One week after insertion of the cannula, the rabbit was used for the experiment. Test materials were injected using a Hamilton 50 μ l syringe with an attachment to deliver 1 μ l at a time. The rabbit's rectal and ear skin temperatures were taken with copper constantan thermocouples and recorded by a Honeywell recording potentiometer. The rabbit was placed in a restrainer for 30 min before injection.

Four materials were injected into the test rabbits. To determine if the cannula was correctly placed, 'Piromen' (Travenol Laboratories, Morton Grove, Illinois), a *Pseudomonas* polysaccharide complex pyrogen, was injected. If the rabbit showed a fever, approximately 1° C rise, within 1 h of receiving 3 μ l of 'Piromen' (50 μ g ml⁻¹) it was used in the experiment. Rabbits were injected with an injectable grade saline solution containing 1% benzyl alcohol (Lilly) to determine if the cannula was clear of bacterial pyrogen and if the injection itself was responsible for the fever. As a control on leukocytic malarial-independent pyrogen, non-infected red blood cells were also injected. Malarial parasites and blood cells were obtained from female ICR white mice. The malaria parasite *Plasmodium berghei* strain NK65DA was transferred by intraperitoneal injection.

The level of parasitaemia was monitored by microscopically examining blood samples stained with Giemsa blood stain.

The blood of both the control and the infected mice was prepared in the same way. The mouse was anaesthetized with ether and the thoracic cavity opened. Heparin solution (0.1 ml), made by adding 0.1 ml of heparin (1,000 USP units ml⁻¹) to 2 ml of saline, was injected intraventricularly. The right lung was then removed and the blood was taken from the thoracic cavity and placed with 0.5 ml of heparin solution. The blood was then centrifuged at 1,000g for 10 min. The plasma and buffy coat supernatant (leukocytes)⁷ were discarded. The

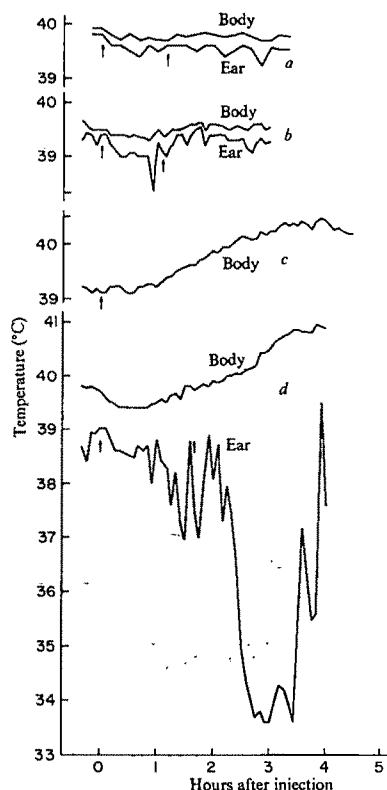


Fig. 1 Direct febrile response to malarial plasmodia. Changes in body temperature and ear temperature of a rabbit following microinjection into pre-optic/anterior hypothalamus. *a*, Saline control; *b*, non-infected RBC; *c*, 'Piromen'; *d*, infected RBC. Arrows indicate time of two injections of 2 μ l in *a*, *b*, and *d*, and of a single injection of 3 μ l in *c*. Saline and washed RBC from mice caused no changes in temperature (*a*, *b*). Bacterial pyrogen, 'Piromen', caused elevation of body temperature to febrile level more than 1 h after injection (*c*). Injection of malarially infected mouse RBC (*d*) causes elevation of body temperature over 1 h after injection. Elevation of body temperature is accompanied by marked decrease in ear temperature indicating vasoconstriction to conserve heat. Ear vessels dilate after 3.5 h as the body temperature stabilizes at febrile level.

packed red blood cells were resuspended with 2 ml of saline of the type mentioned before. The process was repeated four times. The last time the packed red blood cells were suspended in only 0.5 ml of saline and used for injection. The red blood cells were kept in an ice bath at all times except during centrifugation.

Both body temperature and ear skin temperature were within an expected normal range following the injection of saline into the pre-optic region of the rabbit (Fig. 1*a*). Normal mouse red blood cells caused only small fluctuations in ear and rectal temperatures. When the rabbit received malarial infected mouse red blood cells, the rectal temperature rose 1.5°C, and the ear skin temperature fell below 34°C, presumably due to

vasoconstriction in the ear to conserve body heat. The same set of materials, but in varying order, were injected two or three times in each of three rabbits with the same result, no change in body or ear temperature on receiving repeated doses of saline and washed normal mouse RBC, but increased body temperatures of 1.5 to 3°C and reduced ear temperature on receiving infected mouse blood cells or 'Piromen'.

Our results indicate that the presence of the malarial parasite is necessary for fever. The parasite may produce a pyrogen or induce the red blood cell to produce pyrogen. The malarial pyrogen differs from leukocytic pyrogen because the latency of the induced malarial fever is more than 1 h but the latency of the fever induced by a leukocytic pyrogen is about 10 min⁸. The timing and magnitude of the fever from malarial pyrogen resemble the response to the bacterial pyrogen, 'Piromen'. The malarial parasite, however, is a protozoan and eukaryotic and it lacks a cell wall, which is involved in production of bacterial pyrogen⁸. The chemical nature of the malarial pyrogen is unknown, but may differ from the classical division of natural pyrogens into leukocytic or bacterial.

Our studies do not distinguish whether natural malarial fever resulting from lysed red blood cells and plasmodium in the blood activating a leukocytic pyrogen⁹ or a pyrogen produced directly by the parasite is responsible for the fever. In the latter case, malarial fever might differ from the bacterially induced fever. Further characterization of the pyrogen associated with malarially infected red blood cells may yield a product useful for the study of temperature regulation and mechanisms of fever, as well as suggest new clinical procedures for dealing with malarial fever.

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Kidney Graft Survival and Matching for HL-A and ABO Antigens

THIS preliminary report considers 126 kidney transplants from cadaver donors performed in one centre over a period of 6 yr. All were first grafts. Previous sensitisation to human leukocyte antigens (HL-A) had been kept to a minimum by avoidance of transfusion where possible.

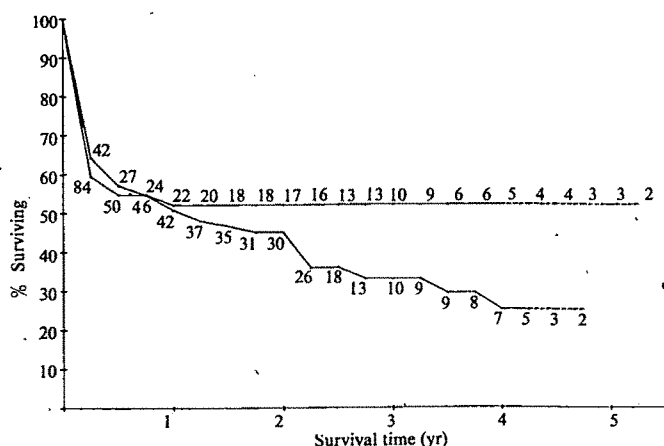


Fig. 1 Actuarial curves of group O and non group O kidney recipients showing total graft failure rate.

Eight patients had weak lymphocytotoxic antibody induced by pregnancy or transfusion before transplantation.

The criterion used for a successful graft at any one time was a kidney supporting life. Rejection was assessed histologically on allograft kidneys, removed surgically or at autopsy, without knowledge of the degree of matching.

Actuarial curves¹ were computed for three, monthly periods using rejection as the criterion of failure. Those kidneys or patients that were lost for reasons other than rejection as assessed by clinical and laboratory examination (as, for example, haemorrhage, ureteric fistula or infection) were censored. Their survival was included in the actuarial curves while they were functioning, but their failure did not contribute to the percentage failure due to rejection. The numbers on the curves represent the number of individuals entering the previous three monthly period.

The HL-A antigens of donors and recipients were assessed at the time of transplantation, and also retrospectively on lymphocytes which had been stored in liquid nitrogen. A panel of well authenticated "monospecific" antisera was used. Many antisera were derived from the IVth International Histocompatibility Workshop. Specificities tested for were: HL-A1, HL-A2, HL-A3, HL-A9, HL-A10, HL-A11, W19, W28 HL-A5, HL-A7, HL-A8, HL-A12, HL-A13, W5, W10, W14, W15, W16, W17, W18, W21, W22, W27. For all except W16 and W21, several sera were used to determine each specificity.

In our study the basic assumptions underlying transplantation practice have been questioned. It is usually accepted that the rules applicable to blood transfusion in relation to the ABO groups also apply to transplantation of the kidney, namely when these rules are contravened, immediate (hyperacute) rejection usually supervenes. It seemed worthwhile, however, to examine whether those ABO categories, regarded as compatible for blood transfusion purposes, also behaved as compatible in organ transplantation. The O allele is believed to produce no antigen on erythrocytes, but it might form an immunogen on tissue cells.

The actuarial curves for the survival of group O recipients (who received kidneys only from group O donors) and non group O recipients of group A, B or AB (who received kidneys from ABO compatible donors) were compared for all graft failures and for failure attributable to rejection (Figs 1 and 2). The survival of group O recipients was better than that for non group O recipients. Rejection failure and survival, when assessed at specific periods, were not significantly different between the two groups. Using the regression method for life tables², however, which assesses differences between the groups over the whole time scale, the log-likelihood ratio is 1.99 ($P < 0.05$).

This suggests that the difference between the survival of group O and non group O recipients is real. The relatively

small number of grafts makes statistical significance difficult to obtain, but a previous series of forty-three grafts performed before HL-A typing was available shows the same trend of superior long term survival of group O recipients. The preferential survival of group O recipients, if real, might be due either to lower immunocompetence of group O individuals to antigens effective in eliciting graft rejection, or to an adverse effect of an incompatibility of the ABO system or an antigen linked with it. The incompatibility, for example, might conceivably be "antigen O" itself, and so a better survival might be expected in the category "donor A to recipient A" than in category "donor O to recipient A". Actuarial curves showed a slightly better survival for the donor A to recipient A group but this was not statistically significant.

We attempted to determine if group O individuals were less capable of responding to HL-A antigens than individuals of other groups. The ABO groups of ninety-four multiparous women who had developed cytotoxic antibody showed no disturbance from expectation. It seems therefore, that antibody produced to HL-A antigens by this immunisation route is not less in group O than in individuals of other groups.

In initial studies with the whole data on first grafts from cadaver donors, the influence of compatibility of the HL-A antigens seemed dubious. There seemed to be an increased survival rate for HL-A identity, but with the small numbers available this did not reach statistical significance.

In group O recipients there were no instances of failure due to rejection, after 9 months, and incompatibilities of HL-A antigens of either the first or second segregant series seemed to have no significant effect on survival.

In non group O recipients there was no significant relationship between rejection and incompatibilities at the first segregant series. A significant relationship did, however, exist between the number of incompatibilities at the second segregant series and rejection in this group (Fig. 3). Grafts having no incompatibilities at the second segregant series survive best, those having two incompatibilities the worst, and those with one incompatibility are intermediate ($P < 0.05$, using the regression method). This reinforces the observation³ that compatibility of the second segregant series is more important than of the first.

Our data suggest that for first grafts, loss of allografts by rejection is less in group O than in other groups, and that for the non group O recipients, matching at the second segregant series produces improved survival. Work in progress indicates that a different picture is presented by second grafts. If confirmed, these trends could make organ donor-recipient matching easier.

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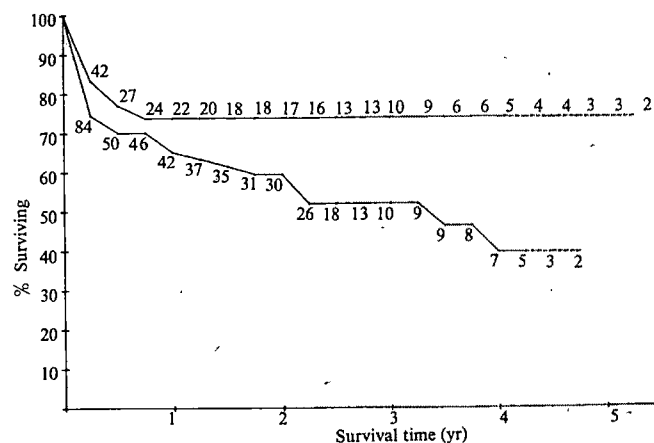


Fig. 2 Actuarial curves of group O and non group O kidney recipients showing failure rates due to rejection ($P < 0.05$).

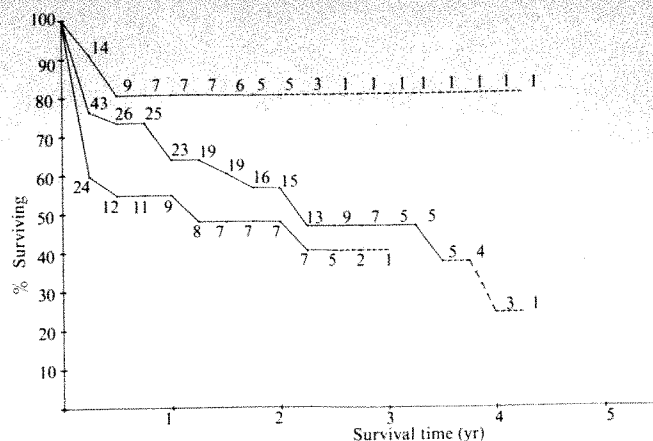


Fig. 3 Actuarial curves of non group O kidney recipients (that is, groups A, B or AB) showing failure rates due to rejection in recipients receiving kidneys with 0, 1, or 2 HL-A incompatibilities at the second segregant series.

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Effect of Sodium Fluoride on Regeneration in the Rabbit Ear

THE unique example of adult mammalian tissue regeneration seen in the rabbit's ear after removal of 1 cm² of its whole thickness¹ has been used to investigate the effects of procedures such as the administration of steroids on this regeneration²⁻⁵.

Sodium fluoride is known to be an enzyme inhibitor⁶⁻⁸ and apparently interferes with carbohydrate metabolism^{9,10} and inhibits cell growth¹¹. The effects of sodium fluoride on regeneration in the rabbit's ear could not, however, be anticipated from the results of these mainly *in vitro* studies. There is contradictory evidence regarding the effects of sodium fluoride on the inflammatory process. It has been suggested that this process, if occurring, is enhanced^{12,13} or reduced¹⁴. The inflammatory process may be an essential precursor to regeneration by the release of a substance or substances necessary for initiating regeneration.

Three groups of mature male rabbits were used: eighteen controls which received London tap water containing 0.3 p.p.m. sodium fluoride; a group of six which received drinking water containing 150 p.p.m. sodium fluoride; and a group of five which received drinking water containing 10 p.p.m. sodium fluoride. All rabbits were anaesthetised with intravenous pentobarbitone, and a hole 1 cm² in area was punched through the whole thickness of each ear with a special punch. Photographs of the ventral surfaces of the ears immediately after the operation (0 d) and at intervals of 7 d up to 49 d were taken with a cm ruler placed alongside the defect. The growth of the regenerated tissue was measured in terms of surface area using the method previously described¹⁵. The regenerated tissue was expressed as a percentage of the initial defect. Any reduction in the size of the hole due to contracture was excluded.

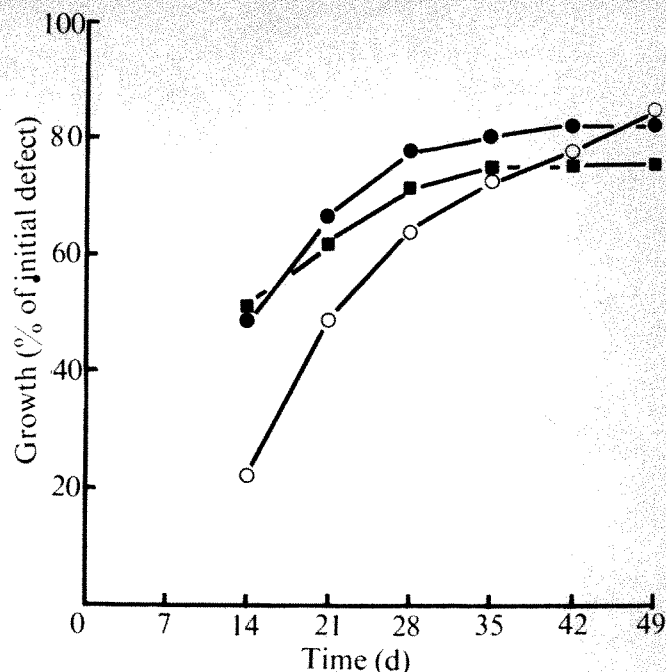


Fig. 1 Comparison of rates of growth at 7 d intervals: ○—○, controls; ■—■, rabbits receiving drinking water containing 10 p.p.m. sodium fluoride; ●—●, rabbits receiving drinking water containing 150 p.p.m. sodium fluoride.

Figure 1 shows the means of the new growth of tissue as a percentage of the original defect in the three groups at 14, 21, 28, 35, 42 and 49 d and Table 1 gives the means and standard errors of the means of the new growth at the same intervals. At 14 d there was a highly significant increase in regeneration in the two groups receiving sodium fluoride as compared with the controls at 14 d ($P < 0.005$). At 21 d the differences were still significant (for the group receiving 150 p.p.m. sodium fluoride $P = 0.001$ to 0.005 and for the group receiving 10 p.p.m. $P = 0.01$ to 0.02). At 28 d the 150 p.p.m. group still showed a significant increase in regeneration compared with the controls ($P = 0.02$ to 0.025) but in the 10 p.p.m. group regeneration was not significantly different from the control group. At 35, 42 and 49 d there was no significant difference between the three groups. (The difference between the 10 p.p.m. group and the control at 49 d was not significant: $P > 0.05$.) In the controls at 49 d, contraction caused about 3% of the reduction in the size of the hole, but in the animals receiving sodium fluoride contraction contributed much more (about 20%) to the decrease in the size of the hole. It should be emphasised that the technique used in this experiment measured only regenerated tissue. Figure 2 illustrates the marked difference in the amount of regenerated tissue seen at 14 d in the control (a) compared with the regeneration in an animal drinking water containing 150 p.p.m. sodium fluoride (b).

These results indicate that sodium fluoride in the doses administered produces a marked acceleration in regeneration

Table 1 Areas of New Growth as Percentages of Initial Defect at Weekly Intervals

Group	No. of rabbits	Mean areas of new growth $\pm$ s.e.					
		Time after excision (d)					
		14	21	28	35	42	49
Controls	18	22.3 ± 3.5	49.1 ± 2.4	63.9 ± 2.8	72.8 ± 2.5	77.0 ± 2.8	85.2 ± 2.6
Sodium fluoride 150 p.p.m.	5	49.2 ± 4.7	67.4 ± 5.2	77.7 ± 4.7	80.6 ± 3.7	83.6 ± 3.8	83.7 ± 3.8
Sodium fluoride 10 p.p.m.	6	50.9 ± 5.1	62.3 ± 3.6	71.8 ± 2.3	74.2 ± 1.5	74.9 ± 1.6	75.3 ± 1.8

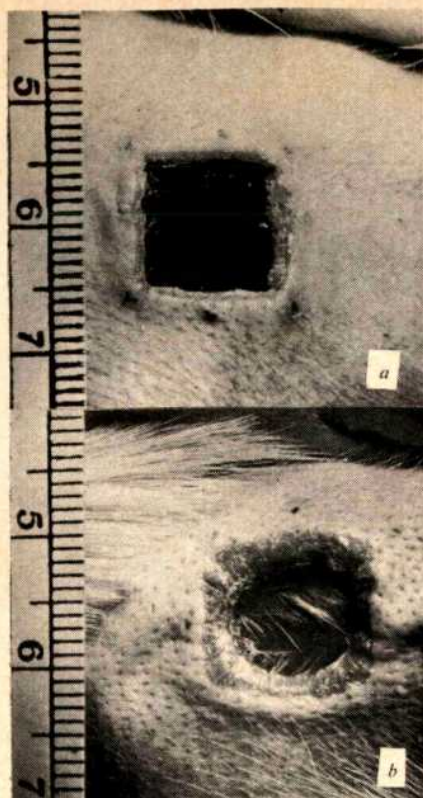


Fig. 2 a, Regeneration in ear of control rabbit at 14 d. b, Regeneration in ear of rabbit at 14 d after drinking water containing 150 p.p.m. sodium fluoride.

during the first three or four weeks following the whole thickness removal of 1 cm² of the rabbit's ear. It is difficult to state how sodium fluoride affects the process of regeneration since the factor or factors stimulating regeneration are not known. Present investigations suggest that at least four enzymes (acid phosphatase, alkaline phosphatase, non-specific esterase and cytochrome oxidase) are not reduced in the region of the blastema although these enzymes are reported to be inhibited by fluoride^{6-8,16}. Regeneration may be stimulated by a wound hormone produced by cell damage following injury and sodium fluoride may increase this early cell damage with the result that the stimulus to regeneration is enhanced. Preliminary investigations suggest that this is the case since there appears to be an increase in the acid phosphatase present 2 d after operation in the fluoride-treated animals as compared with control animals at the same stage. This could be due to increased lysosomal breakdown stimulated by the presence of sodium fluoride.

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Isomerisation of the Visual Chromophore All-trans to 11-cis Retinal

It is well known¹ that the only action of light in vision is the photoisomerisation of the 11-cis retinylidene (derived from vitamin A aldehyde) prosthetic or chromophoric group of rhodopsin, from the 11-cis to the all-trans configuration. After several poorly understood intermediate steps rhodopsin is bleached to opsin, retinal being set free in the all-trans form. Two paths are now possible for the all-trans retinal: either isomerisation to the 11-cis configuration and joining with opsin to form rhodopsin (the situation here, however, is not clear and is likely to be rather complex^{2,3}), or reduction to retinol (vitamin A) and, after esterification, storage as the 11-cis ester⁴.

Since there are six known isomers of retinal, namely all-trans, 9-cis, 11-cis, 13-cis, 9-13 dicis, and 11-13 dicis, the specific isomerization of the all-trans to the 11-cis configuration and the large amounts of the 11-cis form present in the eye⁴ have long been an enigma. Indeed Wald¹ has asked "why should three phyla independently have selected for vision such a fundamentally improbably, hindered cis configuration of retinal (as the 11-cis configuration)?"

In the course of developing a method for simulating *ab initio* molecular-orbital calculations⁵ we have studied all-trans retinal using the results of *ab initio* calculations on relatively large "pattern" molecules including 1,1,3-trimethyl cyclohex-2-ene and crotonaldehyde. The geometry employed is that given by Hamanaka *et al.*⁶ with the modification that all carbon-hydrogen bond distances are set equal to 1.08 Å and the side chain is idealised (that is, the carbon-carbon single and double bond distances are set equal to 1.50 Å and 1.34 Å respectively). This modification allows simulation of the side chain from a small number of pattern molecules. We have found that the results of the simulated *ab initio* molecular orbital (SAMO) method are of comparable accuracy to those that would be obtained by using the much more expensive complete *ab initio* approach. Although the full results of our SAMO calculation on retinal will be published elsewhere we report here some interesting features which may help in understanding the above enigma.

In Fig. 1 we show the numbering scheme used for all-trans retinal. We shall label the occupied π orbitals, in decreasing order of energy, as $\pi_1, \pi_2, \dots, \pi_6$ and the virtual (unoccupied) π orbitals, in increasing order of energy, as $\pi_1^*, \pi_2^*, \dots, \pi_6^*$.

The total overlap populations of all-trans retinal show the π bonding character to be weakest in the region of the C₁₁-C₁₂ bond. From this, in the ground state one would

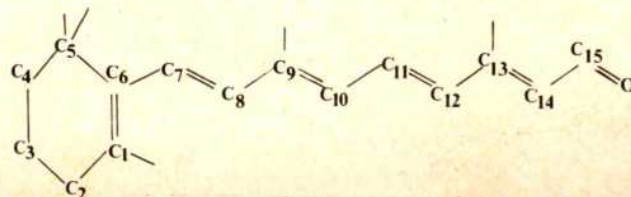


Fig. 1

Table 1 Total Overlap Populations for Various Configurations of All-trans Retinal

Configuration	Bonds			Energy of transition (a.u.)
	C ₉ -C ₁₀	C ₁₁ -C ₁₂	C ₁₃ -C ₁₄	
Ground state	0.23488	0.23180	0.23545	
$\pi_1-\pi_1^*$	0.06285	0.07087	0.12687	0.35107
$\pi_2-\pi_1^*$	0.14382	0.10610	0.10672	0.40001

expect isomerisation to be favoured at this position. This feature, although it has been observed from the much less accurate Pariser-Par-Pople (π electron only) calculation of Pullman and Pullman⁷, has now been confirmed by our more accurate all electron method.

Although the SAMO method produces both occupied and virtual orbital energies for the ground state, since it does not explicitly use electron repulsion integrals, we have been unable to perform configuration interaction calculations. We have, however, been able to estimate the total overlap populations for various configurations. The lowest energy $\pi-\pi^*$ triplet state will best be described by a mixing (configuration interaction) of a number of configurations each formed by the promotion of an electron from an occupied π orbital to a virtual π^* orbital. The lowest-lying virtual π^* orbital, namely, π_1^* , is very much lower (having an energy of 0.02689 a.u.) than the other π^* orbitals. The most important of the configurations describing the $\pi-\pi^*$ excited state will be the $\pi_1-\pi_1^*$ configuration. The next most important will be the $\pi_2-\pi_1^*$. The total orbital populations for these configurations in the ground state are shown in Table 1. Configurations arising from the promotion of an electron from π_1 or π_2 to π_2^* are likely to make very small contributions to the $\pi-\pi^*$ excited state, because of, first, the energy difference and, second, the symmetry of the orbitals locally within the chain. The π orbital population in the $\pi_1-\pi_1^*$ configuration shows that bonds C₉-C₁₀ and C₁₁-C₁₂ are weaker than all other double bonds, the C₉-C₁₀ bond being marginally weaker than the C₁₁-C₁₂ bond. In the $\pi_2-\pi_1^*$ configuration, however, the C₁₁-C₁₂ bond is substantially weaker than the C₉-C₁₀ bond. Thus although we were unable to estimate the amount of mixing of these two configurations, it would seem feasible that there is a sufficient contribution from the $\pi_2-\pi_1^*$ configuration to make the C₁₁-C₁₂ bond the weakest double bond in the excited triplet state.

This leads us to suggest that the preferred isomerisation about the C₁₁-C₁₂ bond is due to the weak nature of this bond in the excited triplet state and that this would be established by a detailed all electron *ab initio* configuration interaction calculation. Such a calculation is economically impossible at present so that the conclusions from our simulated *ab initio* study are of some interest.

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Formation and Breakdown of Aggregations of the Crown-of-Thorns Starfish, *Acanthaster planci* (L.)

IN spite of its notoriety, population densities of *Acanthaster planci* (L.) on most flourishing reefs in the Indo-West Pacific are low. It is possible, however, to find reefs in the region which support aggregations of hundreds or thousands of this starfish¹⁻⁸. In the Sudanese Red Sea we usually found *A. planci* densities of 5 to 20 per km of reef face, but on four reefs aggregations of several hundreds within a few hundred metres were studied⁹. These starfish were not evenly distributed but were usually separated into small subgroups of up to fifteen animals. Such subgroups tended to be associated with favoured species of corals, such as *Goniastrea*, *Turbinaria*, *Montipora* and tabular *Acropora* spp., whose shapes allowed several individuals to feed together and provided shelter from daylight.

We observed that *A. planci* leaving a completely eaten-out *Acropora* table often moved to other tables on which starfish were already feeding, rather than to tables which were as yet untouched. Such observations suggested some form of attraction between individuals. This appeared to influence the aggregation as a whole and our marking studies showed that its integrity was maintained over 3 months, implying some cohesive force. Nocturnal observations were made on the behaviour of two subgroups using tags to identify individuals. In Fig. 1 the mean distances between all the marked starfishes (the proximity index) are plotted against time. This index reveals that within the subgroups, starfishes moved closer together after nightfall once feeding had begun, and it suggests that feeding individuals exert a chemo-attractive influence on hungry starfishes nearby.

To extend our investigations into this possible chemo-attraction mechanism we sought to demonstrate that hungry starfish would select between two alternative food sources provided for them. Preliminary experiments using two large wire mesh Y cages arranged on the seabed were carried out. These allowed hungry starfish to move freely from the shelter of dead corals provided in the stem of the cages, and to choose

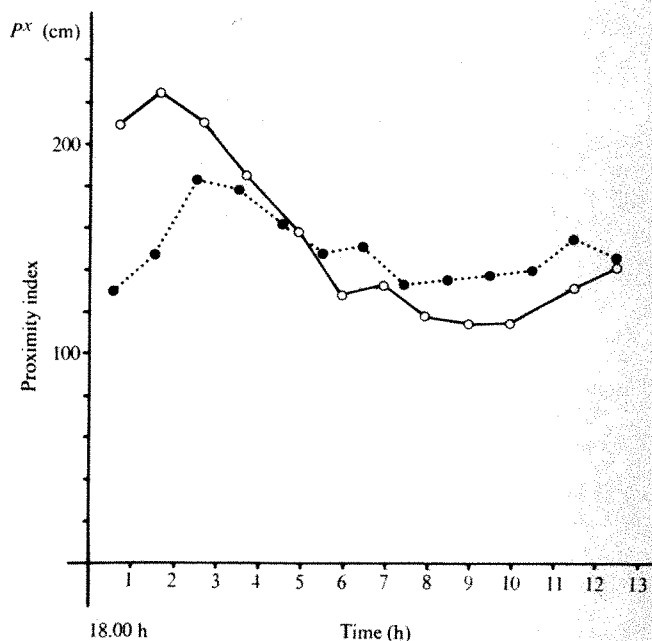


Fig. 1 Variation in the mean inter-starfish distance (proximity index $P^* = \sum |x^i - x^j| / [n(n-1)]$; $i \neq j, i, j = 1, 2, \dots, n$) with time for two groups (○ and ●) of *A. planci* studied at night. The index for both groups decreases after 2 h when some of the starfish had started feeding. The observation areas were 15 m² and there were eight starfish in each group.



Fig. 2 *Arothron hispidus* (L.) feeding on *Acanthaster planci*.

between potential sources of attractant, including other *A. planci* already feeding, located in the arms of the Y. These experiments, which were run at night, indicated an order of preference of attractants in which feeding *A. planci* were more effective than live coral alone, which in turn was more attractive than dead coral.

Because of the mesh structure of the cages, and the possible effects of currents of seawater, it was decided to abandon these tests in favour of a Y maze which took the form of a large aquarium. The base of the Y stem was relatively deep (0.5 m) and allowed seven or more experimental starfishes to hide under shelter during daylight. Seawater was pumped into the arms of the Y maze fresh from the sea. This caused equal currents to pass along each arm, over the attractant sources provided there, towards the base where it flowed out of the system. At dusk the experimental animals became active, and on moving could choose to enter either of the arms. The positions of the alternative attractant sources were reversed from night to night in each experimental series to rule out any inbuilt bias of the maze.

To date, this apparatus has yielded the following results. First, *Acropora* sp. against no attractant: thirty-nine choices to fifteen ($\chi^2=10.67$, $P<0.05$). Second, *A. planci* feeding on *Acropora* sp. against no attractant: thirty-one choices to eleven ($\chi^2=9.52$, $P<0.05$). Third, *A. planci* feeding on *Fungia* sp. against intact *Fungia*: thirty-four choices to fourteen ($\chi^2=8.33$, $P<0.05$).

The first result indicates that *A. planci* navigates towards its prey by chemosensory means like other asteroids (R. J. M., unpublished, and refs 10 and 11) and the second and third show that the feeding activity of *A. planci* on coral releases material which, in favourable conditions, will stimulate other starfish towards its source. This we regard as evidence for our chemo-attraction theory.

Our observations on the chemo-attraction effect in the feeding starfish have led us to propose the following model for aggregation formation. The distribution of low-density populations may be explained as a function of recruitment from dispersed settling larval starfish and the independent migration of solitary adults. An orthokinetic effect³ may serve to influence adult movements, as their rate of progress over the reefs is almost certainly affected by the ease with which they can find adequate food and shelter from daylight.

We found that starfishes preferred areas which were not too exposed to turbulence, not sandy and in which there was an adequate supply of preferred food corals. Within particularly favoured areas the effects of this mechanism, probably enhanced by chemotaxis towards preferred corals, may be sufficient to lead to slight local aggregations. At this state a critical effect seems to operate, for when the starfish come close enough for them to perceive the chemo-attractants described above, the

subgroups of the aggregation form. Local environmental changes may also occur which enhance the development of these subgroups, which we found to develop at densities of thirty to fifty individuals per km of reef face.

We also believe that the activities of an aggregation may influence larval survival and recruitment of juveniles to the population with important consequences in the long term. The increased proximity of adult starfishes may enhance the chances of fertilisation, especially if synchronous spawning takes place as has been described for other echinoderms¹²⁻¹⁴. Further, our group has recently demonstrated that the larvae of *A. planci* settle preferentially among clean calices of some species of coral and also that living corals prey on settling larvae (M. F. Barker, unpublished). Thus, as Cheshier suggested¹⁵, the destructive influence of aggregated adult starfishes will allow an increase in the successful recruitment rate of the juveniles, as in these circumstances larval settlement will not be accompanied by such high mortality. This consideration indicates that the population density of *A. planci* at which aggregation into groups begins may constitute a threshold beyond which a population explosion is likely to occur. The populations of *A. planci* may therefore be particularly sensitive to small changes of significant environmental factors which could result in densities in the region of this threshold; whether as a result of migration and convergence of adults, or due to an initial small increase in juvenile recruitment. Such small changes may be natural or man made.

Our research has indicated that the predatory behaviour of certain species of fish may be important in controlling the densities of adult *A. planci* in the central Red Sea. By continually working under water on one particular reef, many fish became accustomed to the presence of our divers so that their behaviour could be freely observed. Thus, two previously unreported predators of *A. planci* were discovered: the puffer fish *Arothron hispidus* (L.) (see Fig. 2) and the trigger fish *Balistoides viridescens* (Bloch). Both these fish attacked in a characteristic fashion, and the puffer fish left readily recognisable remains in the form of a circlet of detached starfish rays. The trigger fish *Pseudobalistes flavimarginatus* (Rupp), previously reported as a predator of the crown-of-thorns¹⁶, was also seen attacking it in the Red Sea. If these predators respond to an initial increase in the starfish population by feeding more frequently on *A. planci*, they may be capable of an early breakup of an aggregation. Thus if the formation of small aggregations of the type we have been studying is a critical stage in population explosion, these fish predators may be a particularly significant factor in controlling rapid increases in the sizes of *A. planci* populations.

We thank the Overseas Development Administration of the UK Government and the Royal Society who have supported our work. The photograph (Fig. 2) is by P. J. Vine.

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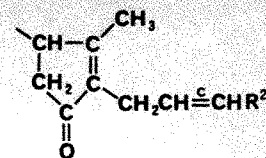
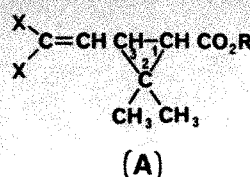
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A Photostable Pyrethroid

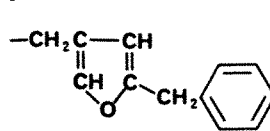
THE natural pyrethrins (see refs 1 and 2 for references) (for example, pyrethrin I (1)) and related synthetic insecticides³ (allethrin (2), bioallethrin (3), resmethrin (4), bioresmethrin (5), Cismethrin (6) and the ethanochrysanthemate (7)) are unstable in air and light (see refs 1 and 2 for references, and ref. 4). This property restricts their use, particularly against pests of agricultural crops, in spite of other favourable characteristics (see refs 1–3 for references) (outstanding potency against many insect species, rapid action, and low mammalian toxicity⁵). We describe here new synthetic esters, ten to one hundred times more stable in light than previous pyrethroids, yet as active against insects as bioresmethrin (5) and with low mammalian toxicity.

A recent modification⁶ of the acid component of bioresmethrin (5)^{7,8} gave a compound (8), 5-benzyl-3-furylmethyl (1R, trans)-2,2-dimethyl-3-(2,2-dichlorovinyl) cyclopropane carboxylate,

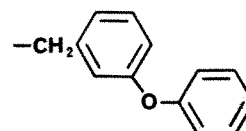


pyrethronyl ($R^2 = -CH=CH_2$)

allethronyl ($R^2 = -H$)



5-benzyl-3-furylmethyl



3-phenoxybenzyl

more potent than most known insecticides (LD50 0.1–0.3 mg kg⁻¹ to houseflies and mustard beetles). Chemical considerations⁹ and spectroscopic evidence indicated that the furan ring in esters of 5-benzyl-3-furylmethyl alcohol was a probable site for photosensitised attack by oxygen (now confirmed for resmethrin¹⁰). Therefore we examined esters of the modified acid with other alcohols. Other esters of potentially photostable alcohols (for example, 2,4-dimethyl benzyl¹⁰, 2,4,6-trimethylbenzyl¹¹, 6-chloropiperonyl¹⁰ and 3-benzylbenzyl¹² even with the most effective acids such as chrysanthemic and ethanochrysanthemate¹³ have been insufficiently active for practical application. In contrast, the ester (9) of 3-phenoxybenzyl alcohol¹⁴ with the 2,2-dichlorovinyl acid was more active against insects than would have been predicted. It was as potent, for example, as bioresmethrin (5) to houseflies and over 2.5 times more potent to mustard beetles; the corresponding (±)-cis,trans esters (11) and (4) had comparable differences in activity. The ester (11) was also three to four times as effective as the corresponding chrysanthemic to *Anopheles stephensi* females and *Glossina austeni* (mixed sexes) (results communicated by F. Barlow).

To determine the stability in light of the new esters, deposits (0.2 mg cm⁻²) were exposed to daylight near a window indoors. In these conditions 50% (determined by gas chromatography)

Table 1 Toxicity of Pyrethrins to Insects and Mammals

Compound	Name or designation	X in (A)	Stereochemistry	R in (A)	Relative toxicities to:		Approximate lethal dose [¶] to rats (mg kg ⁻¹)	
					Houseflies (<i>Musca domestica</i> L.)	Mustard beetles (<i>Phaedon cochleariae</i> Fab.)	Oral	Intravenous
(1)	Pyrethrin I	CH ₃	1R,3R	(+)-pyrethronyl (S at C-4)	2	160	260–420**	5
(2)	Allethrin	CH ₃	Mixture†	(±)-allethronyl	3	1	—	—
(3)	Bioallethrin	CH ₃	1R,3R	(±)-allethronyl	10	4	1,000	4
(4)	Resmethrin	CH ₃	Mixture†	5-benzyl-3-furyl-methyl	42	37	>3,000	160
(5)	Bioresmethrin	CH ₃	1R,3R	5-benzyl-3-furyl-methyl	100	100	>8,000	340
(6)	Cismethrin*	CH ₃	1R,3S	5-benzyl-3-furyl-methyl	41	64	100	6–7
(7)	"Ethanochrysanthemate" [†]	X—X= (CH ₂) ₄	1R,3R	5-benzyl-3-furyl-methyl	140	170	100††	5–10
(8)	NRDC 134	Cl	1R,3R	5-benzyl-3-furyl-methyl	220	260	>400††	26–33††
(9)	NRDC 147	Cl	1R,3R	3-phenoxybenzyl	100	270	—	—
(10)	NRDC 146	Cl	1R,3R + 1S,3S	3-phenoxybenzyl	42	140	>2,000	>270
(11)	NRDC 143	Cl	Mixture§	3-phenoxybenzyl	60	120	1,500§§	>270§§

*NRDC 119, Decis = RU 12063.

†K-othrin = RU 11679.

‡70% (±)-trans, 30% (±)-cis.

§80% (±)-trans, 20% (±)-cis.

|| Determined by comparison of LD50 values from topical application of 1 µl drops of acetone solutions to adults.

¶ For solutions of the compounds in glycerol formal except where stated otherwise. Results communicated by Mr R. D. Verschoyle (compounds (6) and (8)–(11)) or taken from ref. 4.

** Administered in dimethyl sulphoxide.

†† Administered in olive oil. Result communicated by Roussel-Uclaf.

‡‡ For the (±)-trans compound (NRDC 140).

§§ Administered in arachis oil.

of esters (4-7) of 5-benzyl-3-furylmethyl alcohol was lost in 4-6 h whereas the 3-phenoxybenzyl ester (11) lasted longer than 3 weeks. Similar deposits were also exposed out of doors under quartz plates which shielded them from rain and wind but admitted ultraviolet and visible light. In these accelerated tests, where films attained up to 50°C in bright weather, bioresmethrin (5) lasted 1-2 h, compared with about 4 d for the 3-phenoxybenzyl ester (11). Bioassays of deposits with *Drosophila melanogaster* also indicated comparable persistence of insecticidal activity, showing that the photodecomposition products were not toxic to insects in these conditions.

Although such greater stability should extend scope for pest control, persistence of the new esters is moderate and therefore the advantage of freedom from toxic residues should be retained. In addition, their mammalian toxicity is low (see Table 1); for instance, the ($\pm$)-*cis,trans*-dichlorovinyl ester (11) containing about 20% of *cis* component (easily obtained by heating the mixed acid chlorides before esterification), like resmethrin (4), had lower oral and intravenous toxicities to rats than pyrethrin I (1) or bioallethrin (3).

Work is in progress to identify the photodecomposition products and mammalian metabolites of the dichlorovinyl esters and to establish the behaviour of the compounds under practical pest control conditions.

The new compounds are protected by UK Patent Applications Nos 30838/72 and 59184/72. We thank Dr J. M. Barnes and Mr R. D. Verschoyle for communicating mammalian toxicity data, Mr F. Barlow for results with *Glossina austeni* and *Anopheles stephensi*, and the National Research Development Corporation for financial support.

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In the article "Potent Pyrethroid Insecticides from Modified Cyclopropane Acids" by M. Elliott *et al.* (*Nature*, **244**, 456; 1973) two references should be added:

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and so refs 10 and 11 on Fig. 2 should be changed to 14 and 15 respectively.

Erratum

IN the article "Transcellular Strands of Cytoplasm in Sieve Tubes of Squash" by Robert Thaine and Margaret E. De Maria (*Nature*, **245**, 161; 1973) Fig. 2 was reproduced on too small a scale for the salient features to be clearly visible. It is reproduced again here.



Fig. 2 *a*, An electron micrograph from a transverse section of a sieve plate in which pores have a tubular lining of densely stained material. The bar represents 2 μ m. *b*, An electron micrograph from a longitudinal section showing a strand extending from a sieve pore (SP) into the sieve element. W, Sieve tube wall. Black arrow, plasmalemma; white arrow, a group of parallel structures which can be followed from the constricted end of the broken strand (see text). The bar represents 2 μ m.

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BOOK REVIEWS

The Art of Science

From Stonehenge to Modern Cosmology. By Fred Hoyle. Pp. 96. (W. H. Freeman: San Francisco and Reading, March 1973.) £2.10.

AN art historian from Vienna once gave me his personal view of contemporary art—and here I extrapolate freely from memory—that the art of the times is science. He held that some day we will look back on our present science as an essentially religious enthusiasm and the cyclotrons and telescopes that did this science as representative works of folk art.

It is fascinating to read, then, Fred Hoyle's absorbing analysis of Stonehenge as an ancient astronomical observatory. It feels right that the stone age builders of this monument, inextricably close to their environment, should be strongly aware of the eclipses of the Sun and the Moon. It is an intellectual pleasure to follow Hoyle's reconstruction of how the post holes and sighting lines enabled eclipses to be predicted. It was an elevating thought for me to consider that these ancients, with their stone age orrery, had probably a simple, accurate grasp of the spatial relationships of their nearby, celestial neighbours.

But then the question arises: Why did the functions of Stonehenge I decay? Did the early Britons find the smelting of metals more useful than the predicting of eclipses? It now becomes clear that of the four short lectures that comprise this ninety-three-page book, the one on Stonehenge should have come first. The one that is actually first, "Science and Society in Modern Times", should have come second because it raises the question of what makes a society rise and decline. Hoyle notes a tension between science and society. He notes the obvious fact that science, technology and its long range consequences are not deeply understood by many politicians. Hence science is often applied destructively rather than constructively to society. But he does not discuss what is, to me, the more crucial point; that is, the effect of society on scientists. Surely scientists reflect the competitiveness and insecurity of their milieu. They manoeuvre for pre-eminence, squabble over marginal doctrinal issues, and only unite to suppress the threat of new ideas. The real tragedy—beyond the fact that science is not much fun under these conditions—is that science is then misapplied by shortsighted or unscrupulous people from other sectors of society. The scientists have no effective

chance of ensuring that their product is used constructively because they are totally disunited.

If we were ever to live in a healthy, friendly, intelligent world, perhaps the last two chapters in this book would furnish us a glimpse of the kind of activities we would be engaged in. The broadest possible questions are addressed—like the distances of quasars and galaxies, the nature of mass, the phenomenon of seafloor spreading in the Earth. Hoyle faces the hard observational evidence for discrepancies in the conventional cosmology and tries to gain understanding by connecting inferences from many fields of astronomy, physics, and science. Needless to say, his suggestions are considered controversial. It is often said about someone who is obviously very bright, but clearly a non-conformist that, well, maybe he is incorrect but he is valuable because he stimulates thought. That is not quite the point. On many of the issues raised in this book there are right and wrong answers. At least there are some answers that are a good deal more correct than others. About only one thing can we be fairly certain and that is that the *status quo* is incomplete. If we have much of a future, our current understanding of reality will eventually appear extremely primitive. Which are now the most correct answers?

If we progress in our understanding it will have to be through an unprejudiced awareness of our environment. Perhaps the builders of Stonehenge I had such a harmonious attitude toward their surroundings. Perhaps some day we will pursue fundamental questions such as what is the nature of the universe in a more leisurely and co-operative fashion, like an art. And perhaps that will be the most rigorous analysis of all.

HALTON ARP

Buffalo

The Time of the Buffalo. By Tom McHugh with the assistance of Victoria Hobson. Pp. xxiv+339+xi. (Alfred Knopf: New York, December 1972.) \$10.

THIS is a long, in parts detailed but for the most part readable book about both North American subspecies of the so-called buffalo—*Bison bison bison*, the plains buffalo, and *B. bison athabasca*, the wood buffalo. To a much lesser extent it is also about their ancestors and near relatives. It is not clear, however, what readership the author had in mind when writing it, although the somewhat vague, rather nostalgic title

seems to suggest that a wide market is envisaged. This lack of focus may be a consequence of the author's three professional interests: research zoologist with a special interest in animal ecology and wildlife management; author; and photographer for several of Walt Disney's True Life Adventure films, including *The Vanishing Prairie*. It is most certainly not a book for the anatomist, physiologist or palaeontologist and scholars interested in the historical aspects of the buffalo will find that it lacks the depth of Frank G. Roe's *The North American Buffalo: a Critical Study of the Species in the Wild State* (University of Toronto Press, Toronto, 1970).

Much of the book is concerned with the Indians' use of and attitude towards the buffalo at and immediately after the period of first white contacts but it is not a significant contribution to cultural anthropology. The author's real contribution is that, working as an animal ecologist, he has spent considerable time observing at close range the present-day herds in Yellowstone National Park, Wind Cave National Park, the Wichita Wildlife Refuge, the National Bison Range and the Crow Reservation. His objective in doing so was to try to answer some of the "legacy of questions" left by the "vast literature on the beast", not by a further re-sifting of the literature but by personal observations. How did hide-hunters manage to kill large numbers from a single group without frightening the survivors? Did the vast herds wander erratically or make precise annual migrations? Did vast numbers actually die in blizzards, drownings, quicksands and prairie fires? It is from his own observations that the author contributes most in attempting to answer questions like these and it is when he writes of these observations that he is at his most compelling.

Not surprisingly, in the light of the author's professional experience as a photographer, the book is illustrated with some excellent monochrome prints of buffalo in action: at birth and play; wallowing and fighting; and being lured into traps by the author's successful application of the techniques employed by Indian decoys. One would have welcomed more of these, even if it had been at the expense of some of the reproductions of nineteenth century etchings, paintings and photographs of buffalo hunts and hunting techniques. Four pages of maps are given pride of place at the front of the book. These are useful but the two showing the whole of North America lack clarity. There

is a nineteen-page bibliography and the book is generally well produced.

G. MALCOLM LEWIS

Industry and Education

The Universities and British Industry, 1850-1970. By Michael Sanderson. Pp. x+436. (Routledge and Kegan Paul: London, December 1972.) £6.50.

OVER the greater part of the nineteenth century the ancient universities of England were indifferent to industry and did nothing to encourage graduates to take up industrial careers. On the other hand, the provincial universities, founded after 1850, began as science colleges and were always sensitive to the needs of local industry; this was also true of most of the London colleges. By 1914 the universities, including the appropriately reformed Oxford and Cambridge, were able to make considerable technological contributions to the war effort, and they were able to repeat this service during the Second World War. Since 1945 there has been a proliferation of new universities and a great increase in the number of subjects available for study.

Dr Sanderson has chronicled these developments, which I take to be fairly well known, in some detail and he has confirmed most of the conclusions we usually draw from them. He discusses the English university institutions in relation to industry and he has chapters dealing with the Welsh colleges and (particularly interesting) the Scottish universities as well as with special topics such as commercial education and the woman graduate in industry and commerce. He has studied the main sources of support of the universities and has examined the distribution among faculties and subsequent careers of the students. He has sifted an immense amount of material. But there are so many universities and so great is the scope of industry that his work has certain obvious limitations. Apart from Belfast and Coleraine, the Irish universities are not mentioned although they were in the United Kingdom for more than half Dr Sanderson's period. American, French and German institutions come only very marginally into the story, while technical colleges are mentioned only when they become universities. Unsuccessful attempts to found universities are ignored: there is no mention of, for example, the interesting proposal, a hundred years ago, to found a Western University in the Vale of Neath.

Universities, however, do not exist in a social void. The development of British universities, and hence their value to industry, was necessarily restricted by the unsatisfactory state of

primary and secondary education before 1902, the inadequate scholarship ladder and the expense of attending a British compared with a German university. Dr Sanderson does not mention these aspects of the story and he does not comment on the long debate about the role of examinations in university education, to which was related the nineteenth century failure to develop research training. These factors account, in part, for the domination of British industry, and even of British scientific education, by Germans in the early 1900s; a domination that Dr Sanderson notes but does not analyse. Parenthetically, it is notable that the phenomenon was most conspicuous in manufacturing areas of "high technology", such as the Manchester region. The contemporary response included the heroic efforts of Sir Norman Lockyer and the establishment of the British Science Guild.

I am, therefore, puzzled by Dr Sanderson's conclusion that the best British universities had, by 1914, caught up with their German equivalents. Many novel features of British universities in the early years of this century had been explicitly copied from German practice: Imperial College was called the "London Charlottenburg". By 1914 the great majority of professors of chemistry in British universities had German PhD degrees. And, if the situation was by then so satisfactory why was it later thought desirable to introduce the German PhD system into this country?

In fact the tenor of Dr Sanderson's argument is that, generally speaking, we may congratulate ourselves on the way things have gone. Indeed he is almost complacent in his comment that we have avoided the "dualism" of universities on the German model, divided as they are between the traditional and the technological. Surely we are not called on to commiserate with, for example, the Swiss since Zürich is lumbered with both a traditional university and the Federal Institute of Technology?

In short it is not easy to grasp the point of this book. It brings to light no serious problems, hitherto unnoticed, and because of the enormous range of the subject matter it cannot deal in depth with specific issues. I assume therefore that Dr Sanderson intends it as a pilot study and will now go on to make detailed investigations of individual topics. Certainly one hopes that this is the intention; there are, after all, enough problems of modern and of historical importance to deserve the attention of a scholar like Dr Sanderson who is not afraid of hard work and who is capable of dealing with great quantities of intractable material.

The minor criticisms of this book must reflect the interests of the individual reviewer. It is clear to me that Dr Sanderson overlooks the sharp distinction that Whewell drew between "established" sciences (astronomy, mechanics) and "progressive" sciences (such as botany, zoology); it was the latter, Whewell argued, that should not be taught to undergraduates. He is also rather less than fair to Mark Pattison, who became a progressive in his later years and played a part in the "endowment of research" movement. As an adoptive Mancunian I object to Dr Sanderson's cavalier spelling of Fairbairn's name. I think he exaggerates, at the expense of Harwood and Bateman, the part played by Roscoe in the Thirlmere scheme. And, much more serious, he does not mention George Davis, the pioneer of chemical engineering as an academic subject (see his *Handbook of Chemical Engineering*, 1901). Finally, it should be pointed out that only a part of the Royal Navy Signals School, later the Admiralty Signals and Radar Establishment, was moved to Bristol University during the last war; other portions went to places like Haslemere and Witley.

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Wealden Geology

Geology of the Country around Royal Tunbridge Wells. (Memoirs of the Geological Survey of Great Britain, England and Wales.) By C. R. Bristow and R. A. Bazley. With contributions by R. W. Gallois, E. R. Shephard-Thorn, R. Allender, R. Casey and H. C. Ivimey-Cook. Pp. x+161 (9 plates). (HMSO: London, November 1972.) £2.

THE memoir is an explanation of One-inch Geological Sheet 303, New Series, which was resurveyed in 1960–1965 and published in 1971. The area is centrally situated in the Wealden Basin, and at outcrop the solid rocks are almost all of Wealden age with a very small area of Purbeck strata in the extreme south-east. The memoir includes an account of the stratigraphical palaeontology of Jurassic strata penetrated by the Ashdown boreholes, one of which terminated in undated, pre-Jurassic sediments.

After an introductory section, the remaining seven chapters deal with structure, concealed formations, the Jurassic, the Cretaceous, the Pleistocene and Recent deposits, superficial structures and economic geology. Each chapter is composed of individual (initialled) paragraphs by the field surveyors and specialist contributors, which generally fit together well to give a thorough account of the area. An anomaly arises because of the unfortunate use of "Jurassic" and "Cretaceous" as chapter headings: the Purbeck Beds are discussed under the Jurassic despite the apparent acceptance of Casey's views on the age of these beds.

Of the eight chapters, that on the Cretaceous (Wealden Beds) occupies seventy-one out of the 123 relevant pages. There is a general account of the Hastings Beds Group, which is divided into five mappable formations (the term "formation" in parentheses). These represent the deposits of three major cyclothems of deltaic sedimentation. Ostracods provide the most useful zonal fossils, and F. W. Anderson has recognised three *Cypridea* zones. Field mapping indicates that certain stratigraphical names, including "Fairlight Clays", should be abandoned.

Detailed description of Wealden sections occupies fifty-four pages. This contrasts with the brevity of the chapters on superficial structures and on economic geology, which together occupy seventeen pages. For the section on superficial structures a sketch map to illustrate areas prone to surface movement (landslipping, cambering and valley bulging) would have been useful. The chapter on economic geology consists of brief accounts of past and present working for material such as Wealden iron, brick-clay, cement and lime, building stones and oil and gas.

As such it is an interesting historical survey but of limited present day significance. Sand and gravel, for example, are discussed in three short paragraphs, despite the extensive areas of outcrop of sandy formations. Although "no large commercial organisations are utilising this source of sand at present, probably because the sand is too fine for most purposes", an assessment of possible industrial uses, or even of reserves, would be invaluable.

In summary, the authors have produced a good and attractive memoir within the limitations imposed by the standard framework of the sheet memoir series. One is left wondering for whom the Institute of Geological Sciences produces these publications, which have evolved so little in style and content. With the increased emphasis on mineral assessment and other aspects of economic geology within the institute, it could be useful to expand the economic side of the memoirs, possibly at the expense of detailing innumerable local sections.

P. F. RAWSON

Adventurous Physics

Forces and Particles: An Outline of the Principles of Classical Physics. By A. B. Pippard. Pp. xii+321. (Macmillan: Basingstoke and London, November 1972.) £5.75.

PROFESSOR PIPPARD explains in the preface that this book is an expanded version of his lectures to the "fast" stream of first year physics students in Cambridge. He refers to them as "those who wanted the more searching treatment", but certainly in my time the two courses which ran in parallel were referred to as "fast" and "slow". These are relative terms; to quote again from the author's preface, "Recognizing the impossibility of pleasing everyone, I have now addressed myself, as I did when giving the course, to the more adventurous who are prepared to work out for themselves congenial patterns of thought that will make sense of what can so easily remain a disorderly assembly of observations and ideas". This is not, therefore, a book for the average student, and it will not make a fortune for its publisher or its author. It is, however, distinctly possible that it will be an influential book, and it should be read by every physics lecturer, for we are in some danger of forgetting that these topics can be treated with this degree of elegance, economy and clarity.

The coverage is not as wide as the subtitle might suggest; it is restricted to dynamics and electricity and magnetism with brief incursions into relativity and introductory quantum mechanics. A few selected experiments are described in some detail. The order in which,

topics are treated is on the whole not unconventional. I found only one point at which I felt the book departed from the high standard of exposition and logical treatment which characterizes it; this is on page 194 where *D* makes a sudden appearance in circumstances where it might be confused with a depolarizing coefficient *D*, to disappear incidentally after the following page and find no mention in the chapter entitled "Maxwell's displacement hypothesis". There are some characteristically Pippardian asides on topics such as numerology. God, like *D*, is briefly admitted to a possible role (page 130) but is not in the index.

Altogether this is an excellent book in the best traditions of the Cavendish.

W. COCHRAN

A Modern Icarus

Flight and Nature. By M. W. Saunders. Second edition. Pp. vi+126. (M. W. Saunders: Chaldon, Surrey, 1972.) £4.80.

IN a book largely concerned with a theoretical synthesis of man-powered ornithopters, it is strange to find an introduction reiterating all the usual statements on man's ecological responsibilities, however valid such statements may be. The author seems to feel that the study of natural flight is a duty, though he has apparently made no investigations himself. As he puts it: "The main reason for studying ornithoptics and aero-ecology concerns the long term maintenance of our heritage. A broad and continuous investigation would seem appropriate". He also suggests that there is a "likelihood of beneficial offshoots concerning such matters as birdstrikes, aerodynamics, air traffic, etc.". It seems that the author believes that little is known about the flight of birds. His list of references makes no mention of some of the most valuable recent contributions.

The theoretical study is straightforward, though perhaps oversimplified in parts; but where he considers aspects of practical design the proposals are very questionable. There seems to be no realisation of the stresses on the structure, hinge joints, and so on, due to inertial loads. Frictional losses within the mechanism are dismissed; power transfer is supposed to be carried out by wires which the author says must be designed "to have a very low sliding friction. For example, they may slide in guide tubes and be supported: by a fluid medium, by rollers, or by coaxial springs". His proposals for instrumentation are even more obscure: "Information on the craft's performance could be conveyed to the aviator by means of earphones, such information could be verbal, or in the form of sounds related directly with performance.

Direct acoustic connection to the wing surface could be used if preferred".

There is reason for believing that any attempt to achieve man-powered flight by flapping wings must fail. The mechanical limitations imposed by the physiology of the living animal, such as blood circulation and growth, permit locomotion only by the use of oscillatory systems with their inherent problems of inertial forces. Such forces may well set a limit to the size of birds. Man-made devices using rotary motion are not limited by such alternating stresses.

It is true that, as the author says, there is much yet to be learnt about natural flight, but it will not be learnt by this approach.

R. H. J. BROWN

Thinking Computers

Problems of Heuristics. Edited by V. N. Pushkin. Translated from Russian. Pp. vi+202. (Israel Program for Scientific Information: Jerusalem; John Wiley: Chichester, March 1973.) £8.45.

THIS book is a translation—a very competent one—of a collection of papers published by the Institute of Psychology of the Academy of Pedagogical Sciences of the USSR in 1969. It gives one a fascinating glimpse into the current thinking of Russian psychologists about human thought and the problems of describing it in programmatic terms. Apparently there is as much lively discussion in the USSR as in the West of the possibilities and limitations of computer models of psychological processes; whatever the future of artificial intelligence and heuristic programming, it is good to see the issues discussed in such a thoroughgoing fashion.

The authors represent a wide variety of disciplines, including psychology, logic, pure mathematics and engineering. Their interests are reflected in the structure of the book, which is divided into four parts. Parts 1 and 2, entitled "Theoretical Problems and Heuristics" and "Experimental Studies and Heuristic Processes" respectively, are intellectually dominated by the editor's own contributions. He sees clearly the need to study human performance in order to construct effective algorithms for automatic process control and problem solving, and draws attention to the serious deficiencies of "stimulus-response" automata as models of human problem solving. What we need, he suggests, is a theory of "heuristic automata" which could model the elements of a given problem, construct systems from these elements and use the systems for solving the problem. Unfortunately there is no general theory of such automata at the present time.

The other two parts of the book are entitled "Programming and Components of Human Thought" and "Investigation of Reflexive Processes". The latter is the

shortest section and the most idiosyncratic; it deals with "devices which optimise their performance in response to human counteraction", and it is not clear that they have very much to tell us about human thought. But the main body of the book, represented by parts 2 and 3, is a mine of case studies of human beings attempting to solve simple (and not so simple) intellectual problems. There is a thoroughly professional chapter on the perception and recollection of board positions in chess, this study being backed up by observing the eye movements which accompany the examination of a board position in the process of attempting to memorise it or to solve a chess problem. There is a comparison between the performance of humans and computers in solving various kinds of rearrangement puzzles and a very long chapter on the famous problem of the fly which travels to and fro between two cyclists riding towards each other—though perhaps it generates more amusement than psychological insight. In part 3 the most interesting paper is one on the automatic design of pipelines, an exercise in cooperation between human designers and computing machines. It seems to be inspired by a good sense of the proper place for computers in human society.

H. C. LONGUET-HIGGINS

Medical Thoughts

Medicine and Society. By H. Miller. Pp. 87. (Oxford University: London, August 1973.) £2.25 library edition; 80p paper.

THIS is an excellent book that ought to be read by anyone with the slightest interest in medicine and medical services. In eighty pages Dr Miller gallops through (*inter alia*) drug development, operation of the National Health Service, staffing of hospitals, general practice, population screening, education, dentistry, genetics, abortion, euthanasia, transplants, contraception and the medical needs of the third world. He says something interesting and provocative about them all, and doesn't waste a word.

The Medical Research Council and molecular biology are rapidly dispatched in "it is still difficult to escape the impression that the collection of Nobel prizes and the headlong pursuit of the almost metaphysical harvest of molecular biology has taken precedence over the exploitation of science in the service of medicine and man". He clearly dislikes any thought that euthanasia might be available through the medical profession: "It might be more appropriate for an enthusiastic prelate to conduct the patient to the Elysian fields".

This is just the book for a ninety-minute train journey.

DAVID DAVIES

Rationalizing Water

Scientific Allocation of Water Resources: Water Resources Development and Utilization—A Rational Approach. By Nathan Buras. Pp. 208. (American Elsevier: New York; Elsevier: Amsterdam, 1972.) Dfl.46; \$14.50.

THE last decade has seen both a much greater awareness of the many severe and growing complications (technical, legal and social) in water resources studies and the development of powerful systems engineering techniques. The techniques, however, cannot yet cope fully with all the complexities of the overall water resources problem. Either the problem has to be simplified in certain aspects or the techniques are applied to particular components of the overall problem.

In the latter category, Buras has made notable contributions to the development and application of systems techniques in water resources engineering. His book shows succinctly (in 200 pages) his authoritative grasp of the subject and is to be welcomed for bringing together material dispersed over a plethora of journals and proceedings.

The preface and introduction give respectively lucid surveys of the book itself and of the historical background of water resource development from Biblical times onwards. The overlap of water resources engineering with many related disciplines in the pure and applied sciences and in the social sciences is well summarized in the introduction.

Chapter 2 sets out the philosophy of the systems approach to water resources studies, without obscuring that philosophy with mathematics. Summaries of applications of the approach in California, the Indus Valley and Israel are presented. Wisely, Buras stresses that the application of systems engineering to water resources problems is only in its initial exploratory stage.

After distinguishing between development problems, design problems and operational problems in chapter 3, he gives a full account of those probabilistic methods applied in water resources studies, with the minimum of mathematical obscuration, in chapter 4.

The optimization techniques widely used in water resources problems, and to which Buras has himself made many contributions, are set out in chapters 5, 6 and 7. Linear programming, with specific examples to lighten the basic material, is adequately covered in chapter 5. The main value of the whole book, however, may well be the thorough treatment given to dynamic programming methods, both as a way of approach and in their application, in chapters 6 and 7. These chapters seem to me to be the outstanding feature of the book, and will provide a sound insight to this complex subject. A brief

review of simulation methods is given in chapter 8.

This book fills a gap in the texts on water resources engineering. It deserves to be studied by all graduate students in the water resources field, and should be read by many others in the associated disciplines.

T. O'DONNELL

How Herbicides Work

Mode of Action of Herbicides. By Floyd M. Ashton and Alden S. Crafts. Pp. 504. (Wiley Interscience: New York and London, February 1973.) £12.50.

THIS book is a mine of information. It opens with a few general chapters on the economics of weed control and on the classification of herbicides and then proceeds to give brief comparative consideration of factors affecting uptake and translocation of herbicides, on their molecular fate in the plant and on the main kinds of biochemical responses of plants to their presence. This is followed by fifteen chapters, together occupying the greater part of the book, each dealing with a chemically defined group of related herbicides.

Each of these specialized chapters is arranged on a common plan. First, the herbicides themselves are defined and described. Next, their general macroscopic effects on plants are outlined and our knowledge of their uptake and translocation is summarized. Then follow sections on metabolic change of the herbicides in the plant, if any, and on the known biochemical responses of the plant in the period preceding death. This latter is usually the largest section in each chapter. A final section summarises present views on which of the induced biochemical abnormalities are most clearly associated with plant death. Each chapter is provided with a well chosen set of references so that any point of special interest to the reader can be easily followed up.

The modern herbicides are virtually all products of the last thirty years or so; it is really notable how much work has been done on their physiological and biochemical effects. Two main observations can be made on the results of this work. First, it is clear that very few herbicides indeed have a simply definable mode of action, at least in our present state of knowledge. Perhaps the best example of a simple mode of action is that of the nitrophenols; these compounds have been well known to biochemists for a long time as uncoupling agents and it seems that it is indeed this activity which is mainly responsible for their toxicity to plants. At the other extreme, the phenoxy-acetic acid hormone-type weed killers induce an enormous number of unrelated biochemical responses and we are still, after thirty years research, far

from being able to account for their important herbicidal activity.

The second general observation is that it is striking that few, if any, herbicides show a true specificity of action. Selectivity, when it occurs, is often based on crude mechanisms based on differential wettability of leaf surfaces, ease of uptake and translocation or access to root systems. Sometimes a more sophisticated mechanism is involved where selectivity is based on differential capacity to degrade the herbicide to less toxic derivatives. Specificity based on action at a specific site is not known, contrasting in this respect with some of the more selective antibacterial antibiotics.

This is a book which will interest not only the specialist working on herbicides but also many with a more general interest in the action of toxicants on living cells. It is a book that many would like to have as a reference book on their own shelves, but the price is scarcely encouraging.

P. W. BRIAN

Coastal Problems

The Water's Edge: Critical Problems of the Coastal Zone. Edited by B. H. Ketchum. (Coastal Zone Workshop held 22 May–3 June, 1972, Woods Hole, Massachusetts.) (MIT: Cambridge, Massachusetts and London, 1972.) £1.80; \$3.95.

A RECENT review of scientific, economic, social and political problems of coastal zones has been published from MIT—a result of a “workshop” jointly sponsored in 1972 by the US Institute of Ecology and the Woods Hole Oceanographic Institution and supported by NSF (RANN Program) and the Rockefeller Foundation.

As Hollings¹ has observed of another, similar exercise “the real success of the workshop rests as much with its style of operation as with its substance” but of its method of operation the book gives little clue. Chapters have been prepared by small, presumably editorial, groups, with “contributions from . . .”. This technique provides a pleasant uniformity of style, but one wonders how much dissension, argument and genuine difference of view has been incorporated.

The report considers, in turn, diverse aspects of coastal zone problems—those arising from cropping biological resources; from non-renewable resources of oil, gas, minerals, gravel; those posed by growing demands for recreation and amenity; those changes brought by urbanization, industrial development, navigation and waste disposal schemes.

It effectively distinguishes between exclusive uses of the resource (such as aquaculture, or nature reserves), multiple uses (such as water for industry, waste disposal) and displaceable uses (that is, those such as power stations which could

be located elsewhere), and sagely observes that the present sad state of many coastal sites is a result of their non-management as much as mismanagement.

From the British standpoint both comparable and contrasting views are indicated. First, the coastal zone is “a band of dry land and adjacent ocean space”—in effect extending over coastal plains, or even whole watersheds, to the edge of the continental shelf and beyond. The United Kingdom concept of coastal areas, by contrast, appears parochial, if more closely focused. Perhaps inevitably, the same conflicts of use emerge in both the USA and UK, and there is the same divisive confusion of land use planning, management and legislative authorities. It becomes a truism that integrated and well-managed use of these areas demands a closely knit, well co-ordinated, overall agency, vested with suitable powers to make decisions effectively, and with the wisdom of a Solomon, to boot.

In a series of far-reaching recommendations the MIT reports calls for: a national coastal zone policy to determine priorities for future uses and to maintain natural ecosystems; a coastal zone task force to develop management schemes and model guidelines for regional and local plans; for revision of legal institutions and procedures to make management more effective; for establishment of coastal zone centres to carry out and coordinate scientific, social and legal research programmes; for a national system of coastal area preserves with closely restricted access, to protect basic genetic stocks.

The problems exposed are those we face nearer home, the ideal solutions much the same as those we would choose: will the Americans be more successful than we in devising a fair, rational and effective scheme of regional control? The cards seem stacked against them: to quote: “67% of California's estuarine habitats lost in twenty years”; “of recreational shoreline, 92% was privately owned”; “booming coastal industry” which includes increased dredging and filling, increased developments in underwater mining and oil extraction.

UK problems of the coastal zone have been considered, in part, by the Royal Commission². The new Regional Water Authorities will be able to tackle some effects of our present disorganization, but will be short on skills and resources in the aquatic field, at least initially, as well as restricted in the scope of their interest. Surely the need is now for the UK to look at wider aspects of coastal zone management. The growing offshore extraction industries and our developing links with other riparian countries bordering coastal waters will present

many problems in the years ahead that a rational management scheme could overcome. Perhaps the Royal Commission could extend its sights beyond estuaries, to the coast and nearshore waters, to identify important issues and to achieve an overall assessment of our needs, both now and in the future.

The MIT report represents a rational and sensible approach to these problems, and no one sector has been able to press its own problems at the expense of the others. This, in essence, is the virtue of the openness and flexibility of the workshop approach. But the shining ideals and grand concepts need both the will, the machinery, and the funds to advance further. The provision of these, both in the UK and US, is where the real challenge lies.

G. HOWELLS

¹ "Resource Science: The nurture of an infant", *Bioscience*, 23, 13 (1973).

² Third Report of the Royal Commission on Environmental Pollution, Cmd 5054 (HMSO, 1972).

Activities of Wasps

The Wasps. By H. E. Evans and M. J. W. Eberhard. Pp. vi+265. (David and Charles: Newton Abbot, July 1973.) £3.65.

THE wasps are all those sting-bearing or aculeate Hymenoptera which are not ants or bees. About half of these are wasps in the more restricted sense—species which build nests and store food in them for their young. The ability to display this degree of maternal care involves many new behavioural traits; having a nest, for example, means having a sense of locality and a good memory and these in turn make such wasps a fascinating study because of the contrasts between some quasi-human behaviour and much rigid instinctive activity.

Dr Evans is an authority on the diggerwasps, a large group of solitary species on which he has published much original work. They show all stages from the simplest in which the wasp stores paralysed prey and lays an egg on it but then seals the cell to such species as *Amonophila pubescens* which brings her larva food as required, over several days, and is able to run two nests simultaneously, in different stages of development and requiring different treatment.

The other author, Dr Eberhard, has made brilliant studies of *Polistes* wasps. The colonies of these insects are very convenient for observation, the single combs being usually completely exposed, often hanging from the eaves of houses and the colonies being mostly small so that the individuals can all be marked with paint and their activities separately recorded. Species are found in both temperate and tropical climates and the

resulting differences in behaviour enable us to see better what elements are fundamental and what are adaptations to local conditions. Thus in temperate climates only the fertilized females survive the winter while the males and workers die. To survive, the female has to be rather larger and to lay down a fat reserve of a rather different form. In the spring she can found a new colony unaided until her first daughters emerge. In the tropics, colonies would be perennial except that, when the dominant egg-laying female begins to fail, the colony disperses, usually founding new colonies with swarms.

It is not yet certain that in such species there is any distinction between egg-laying female and workers except a behavioural one, the egg-laying female being able to prevent the others from laying, so that they become workers by default. In such wasps there is still need for research to settle whether there is a caste of real workers which could not alone found new colonies. The more advanced social wasps which are also described often make much larger nests with a beautiful and elaborate structure, inhabited by thousands of wasps which in some genera may include a large number of egg-layers. In these wasps the egg-layers are sometimes quite distinct and easily distinguishable from the workers to the naked eye, as in the British social wasps. All these and many other topics are ably and lucidly discussed in this valuable introduction.

O. W. RICHARDS

Motile Models

Motile Muscle and Cell Models. By N. I. Arronet. Translated from the Russian by Basil Haigh. (Studies in Soviet Science.) Pp. ix+192. (Consultants Bureau: New York and London, 1973.) \$29.

THE title of this unusual book may mislead the prospective reader. What constitutes a model of a muscle or motile cell? By a model one often means a physical object or a mathematical theory which reproduces the important properties of a more complex system. But in the present context, model is used in the sense of a copy of the original. In 1946 Varga in Szent-György's laboratory introduced the glycerol-extracted muscle fibre as a model of a living muscle. Treatment with glycerol destroys the cell membrane or greatly increases its permeability and removes metabolites and soluble enzymes. What remains is a working model of the muscle which can be manipulated by the experimentalist since it is permeable to substrates and inhibitors of the contractile proteins. Whether the properties of the model reproduce those of the living muscle must be determined by experiment.

Because the contractile proteins are relatively insoluble the model has proved to be a remarkable likeness of the original. Nevertheless there are differences, particularly in regard to inhibition of ATPase activity in the relaxed state.

The preparation of a glycerinated model is a simple technique, and has consequently been applied to a variety of presumed motile systems, including cilia, sperm, dividing cells, amoebae (and other organisms which exhibit protoplasmic streaming), myonemes of *Vorticella* mitochondria, and chloroplasts. The criterion for a successful model is simply the production of some form of movement on addition of ATP or other substrates. If the original is a highly ordered structure whose mechanical properties have been determined, one can establish that the model is a reasonable copy of the original. The technique has been successfully applied to cilia and flagella particularly by Gibbons who has obtained wave propagation and swimming movements with glycerinated sperm. For other systems it is difficult to decide whether the essential properties have been preserved and whether the response observed bears any relation to the normal function.

Arronet's book is a survey of studies on glycerinated models of all kinds. One use of models is for teaching purposes and perhaps the most interesting feature of this book is a collection of recipes for making models. Practical details are stressed and many of the methods seem to have been tested by the author.

The remainder of the book is a review of the literature on model studies. The presentation is more in the form of a recitation than a critical discussion. As long as the model is prepared from a muscle or cilium, one is on relatively firm ground, but for other systems extreme caution is required. Discussion of work on mitochondria and chloroplasts will serve as an example. Addition of ATP to these organelles, whether glycerinated or not, can lead to changes in shape and volume. The presence of a myosin-like contractile protein has been claimed and denied by a number of workers and at present it seems likely that the volume changes can be explained by ion movements. Yet Arronet concludes on the basis of ATP response of glycerinated mitochondria and chloroplasts that they "share a common mechanism of contraction with muscles, enzymatic interaction between the contractile protein and ATP".

Glycerinated models have been and will continue to be an important method in the study of motile systems. This book provides a useful collection of such studies and will serve as a valuable reference.

E. W. TAYLOR

CORRESPONDENCE

Smoking and Pregnancy

SIR,—Some of us decline to accept Dr Goldstein's own evaluation of his criticisms¹⁻³. He states³, as an "undisputed" fact, that "... the distribution of birthweights for babies of smokers is the same as that for non-smokers except that it is shifted downwards by about 170 g". (This is known as the 'displacement hypothesis'.) It follows that the mean birthweight of infants born to smoking mothers should also be "about 170 g" less than that for babies born to non-smoking mothers. In Yerushalmy's study⁴, the observed differences in the mean birthweights were 209.1 g for "whites" and 204.8 g for "blacks". By suitably stretching our imaginations we can, perhaps, regard these as being "about 170 g". However, Yerushalmy⁵ also tested the hypothesis that the distributions of low birthweights, allowing a displacement of 200 g between the smoking and non-smoking series, are the same. He found that the distributions differ significantly ($0.005 < P < 0.01$). The 'displacement hypothesis' is therefore rendered improbable by Yerushalmy's⁵ findings.

So much for "undisputed" facts. Apart from raising doubts about Goldstein's most confident assertions, they do not affect Yerushalmy's arguments. To quote Yerushalmy⁶, "... the major conclusions in the paper (ref. 4) do not rest on the results of the displacement hypothesis". In particular, contrasts between the findings for infants of smoking mothers and smoking fathers cannot easily be reconciled to a cause-effect hypothesis⁴. Although smoking mothers, and especially smoking fathers, had a higher incidence of low-birthweight babies than corresponding non-smokers, prognosis (death and congenital anomalies) for the low-birthweight babies of smoking fathers was much worse than for low-birthweight babies of smoking mothers⁴. By far the best prognosis was given for infants of matings in which the mother smoked and the father did not. This finding applied both to "whites" and "blacks". Furthermore, the general unsoundness of arguing from simple association to cause was emphasised by the large biological and mode-of-life differences demonstrated between smoking and non-smoking gravidas.

Now to answer Goldstein's second point³. Yerushalmy⁶ found that women who began to smoke after the birth of their baby had a much higher incidence ($\times 1.8$) of low-birthweight babies than those who did not take up smoking. His investigation was confined to all

births that occurred in women aged twenty-five or less, and in women who started to smoke in this age-range. Goldstein³ argues that the observed difference in the incidence of low-birthweight babies arises because mothers who started smoking before twenty-five years of age would have had their babies at an earlier age than those who did not take up smoking: younger mothers, he claims, have lighter babies. Yerushalmy⁷ has previously shown that his findings do not support this objection: "... within the limited range of ages under twenty-five years the variation in the proportion of low-birthweight infants is very small and could not account for the large differences found." He supported his argument with a table showing the mothers' age, total live births, and the numbers and incidence of low-birthweight infants⁷. We can split the age-range conveniently into two groups to give equal numbers (164) of low-birthweight infants: for mothers in the age-range fifteen to twenty-one years, the incidence of low-birthweight babies was 6.2% (164/2639); and for those in the age-range twenty-two to twenty-five it was 5.6% (164/2906). The small difference does not approach significance (χ^2 with Yates correction = 0.71; $0.3 < P < 0.5$). By contrast, the differences in the incidence of low-birthweight babies born to mothers in different smoking categories were large and significant. For "white" non-smokers, the incidence was 5.3%, but for "white" mothers who took up smoking after the birth of their baby it was 9.5% ($P < 0.01$)⁶. The corresponding incidence⁶ for mothers who smoked during pregnancy was 8.9%; and for those who gave up smoking after the birth of their baby it was 6.0%, similar to that for non-smokers. Trends for "blacks" resembled those for "whites", but because of smaller numbers, the only statistically significant difference was between those mothers who gave up smoking after the birth of their baby—with an incidence of low-birthweight babies of 13.4%—and those who smoked both during pregnancy and afterwards—with an incidence of 19.9% ($P < 0.02$). This collective evidence⁶ therefore fails to corroborate the causal hypothesis. Each of its features is remarkably consistent with the view that the smoker, rather than the smoking, is responsible for the high incidence of low-birthweight infants^{6,7}.

Finally, I return to the questions raised in your editorial of September 14. A news story based on an accurate

report of an article by Goldstein opened with the statement that cigarette smoking during pregnancy "caused the deaths of 1,500 babies in Britain last year". Under pressure from your leading article, Goldstein conceded in these columns, on October 5, "... the scientific evidence for a causal relationship may not be very conclusive". These dual standards raise important issues.

The public should be able to trust definitive statements made by scientists in their own field of expertise. If subsequently this trust proves to be unfounded, the credibility of scientists will be undermined, not only to their detriment, but to that of society at large.

Yours faithfully,

P. R. J. BURCH

Department of Medical Physics,
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¹ Goldstein, H., *Am. J. Epidemiol.*, **95**, 1 (1972).

² Goldstein, H., *Am. J. Obstet. Gynec.*, **114**, 570 (1972).

³ Goldstein, H., *Nature*, **245**, 467 (1973).

⁴ Yerushalmy, J., *Am. J. Epidemiol.*, **93**, 443 (1971).

⁵ Yerushalmy, J., *Am. J. Epidemiol.*, **95**, 2 (1972).

⁶ Yerushalmy, J., *Am. J. Obstet. Gynec.*, **112**, 277 (1972).

⁷ Yerushalmy, J., *Am. J. Obstet. Gynec.*, **114**, 571 (1972).

SIR,—We join Professor Burch¹ in welcoming your leading editorial² on "smoking, pregnancy and publicity", and for noting that the elementary fallacy of inferring causality from statistical association is present in some reports that have received publicity.

In response to your editorial, Goldstein³ cites a *British Medical Journal* editorial⁴ that he states "suggests" validity of the smoking-causality hypothesis as an explanation for the statistical association between smoking behaviour of women and birth weights of their children. An alternative hypothesis, set forth by Professor Yerushalmy, is that the smoker rather than smoking influences birth weight⁵. Another expression of this hypothesis is that "smoking behaviour of women and birth weights of their children are influenced by a common cause ... the individual genotype or constitution"⁶. The *British Medical Journal* editorial⁴ does not merely suggest, but asserts that "no reasonable doubt now remains that smoking in pregnancy has adverse effects on the developing foetus". As we have noted⁶, the editorial overlooked

several reports that disagree, especially those of Yerushalmy.

Ross and colleagues⁷, and Goldstein⁸, deny having inferred causality from correlation. To the causal quotation cited in the *Nature* editorial² may be added their own assertion⁸, based on statistics, that "cigarette smoking during pregnancy increased the foetal plus neonatal mortality rate by 28% and reduced birth weight by 170 g. . . ." They also assert⁷ that the constitutional hypothesis as evaluated by Yerushalmy⁵ "suffers from severe methodological shortcomings, making it clearly untenable", citing a critique by Goldstein⁹. However, they neglect to mention Yerushalmy's rejoinder¹⁰ which, in effect, demolished this critique⁹.

Goldstein expressed his opinion that it would be "unethical" not to advise and encourage "pregnant women, especially 'high risk' ones, to stop smoking"¹³. In response to similar statements by Goldstein⁹, Yerushalmy¹⁰ commented, following a data analysis, that it would be unfortunate "to recommend a course of action based on conjectures, subjective notions, and easy explanations not supported by available data." The smoking-causality hypothesis to explain the association between smoking by women and birth weights of their children is incompatible with observed data^{5,6}. Such incompatibility, if confirmed independently, requires rejection of this hypothesis.

A problem arises since human smoking behavioural subgroups, for example, smokers, non-smokers and ex-smokers, are self-selected rather than randomly selected, and thus are biased samples. This introduces special problems for statistical testing of hypotheses^{5,6}. It is quite possible that for a subgroup of all smokers, tobacco use may be symptomatic of underlying

needs, perhaps arising in part from variations in biogenic amine physiology, that tend to be alleviated by nicotine^{6,11}. Cigarette smokers tend to adjust their smoking behaviours according to the nicotine content of cigarettes¹². Accordingly, ethological homeostatic mechanisms may be involved^{6,13}.

Goldstein cites animal studies in support of his position⁸. In addition to the usual caveat concerning inferences from experimental animal studies to man, based on interspecific physiological differences, there is a further problem. If habituated human smokers are on the average physiologically different from non-smokers, this difference may not be reflected in the physiology of experimental animals used in tests. Moreover, biogenic amine release in non-deficient test animals above homeostatic optimal ranges may be harmful¹⁴. The fallacy of typology¹⁵ may well be involved.

Consider the following observations: the negative association of carboxyhaemoglobin (COHb) levels of women with birthweights of their children¹⁶; the low COHb levels of some smokers^{16,17}, and the limited data for angina patients showing that high COHb levels of smokers are sustained during a non-smoking period¹⁸. These are compatible with a constitutional rather than a smoking-causality hypothesis. Such observations suggest caution regarding rejection of constitutional hypotheses and allegations that smoking-causality hypotheses concerning birth weight are in fact true. In this complex problem, available objective evidence for testing alternative hypotheses must be considered fairly, without overlooking critical reports that are detrimental to the smoking-causality hypothesis⁴, or to any other hypothesis. It is to be hoped that in any scientific problem all avail-

able objective evidence may be utilised, thus minimising the need for subjective judgment and opinion.

Yours faithfully,

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¹ Burch, P. R. J., *Nature*, **245**, 277 (1973).

² *Nature*, **245**, 61 (1973).

³ Goldstein, H., *Nature*, **245**, 277 (1973).

⁴ *Br. med. J.*, **1**, 369 (1973).

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¹¹ Hickey, R. J., Clelland, R. C., and Harner, E. B., *Lancet*, **i**, 270 (1973).

¹² Frith, C. D., *Psychopharmacologia*, **19**, 188 (1971).

¹³ Hickey, R. J., Harner, E. B., Clelland, R. C., and Boyce, D. E., *Naturwissenschaften*, **60**, 206 (1973).

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¹⁸ Hickey, R. J., Clelland, R. C., and Boyce, D. E., *Lancet*, **ii**, 571 (1973).

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QUALIFICATIONS. A Ph.D. degree in engineering or physics and demonstrable research ability, together with a thorough background of electromagnetic theory and aerial and guided wave techniques. Practical experience in these fields would be an advantage.

SALARY. The appointments will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A8,489-\$A12,932 p.a. An outstanding applicant may be offered appointment at a higher level.

TENURE. Either an indefinite or fixed term appointments may be negotiated. Indefinite appointments carry Australian Government Superannuation benefits.

Applications, stating full personal and professional details, the names of at least two professional referees and quoting the appropriate Reference Number should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64-78 Kingsway, London WC2B 6BD.
by the 14th December, 1973.

Applications in U.S.A. and Canada should be sent to:

The Counsellor (Scientific),
Embassy of Australia, 1661 Massachusetts Avenue, N.W.,
Washington, D.C. 20036, U.S.A.

(1584)

ELECTRON MICROSCOPE TECHNICIAN Grade 3 required for Biological E.M. Unit containing 3 transmission and one scanning unit. Candidates with experience of scanning electron microscopy preferred. Day release available. Salary Grade 3 £1,650×54-£1,920 p.a. plus £175 p.a. London weighting. Five-day week, five weeks (in total) annual leave.—Letters only to Assistant Secretary (Establishment) (N), Queen Mary College, Mile End Road, London E1 4NS, stating age, experience and qualifications. (1540)

ROYAL POSTGRADUATE MEDICAL SCHOOL. SENIOR TECHNICIAN required in Department of Medicine. The appointee will assist in a research programme concerned with the detection of early bronchial disease by sensitive physiological tests. Qualifications HNC in physiological measurement or equivalent. Salary in range £1,473-£2,169 per annum, according to qualifications and experience.—Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 2/213/N. (1558)



BBC NATURAL HISTORY UNIT

requires

PRODUCTION AND RESEARCH ASSISTANTS

To work on a wide range of Natural History Television Programmes, initially the "World About Us".

Production Assistant, (Ref. 73.G.924N)

Will be required under direction to research, suggest and write treatments and help produce and direct film or studio programmes. Experience of television production and a knowledgeable interest in Natural History or Biology essential. Appropriate degree desirable. Based Bristol.

Salary: £3,123 p.a. (may be higher if qualifications exceptional) × £156 to £3,903 p.a. plus £195 p.a. non-day working allowance.

Research Assistants, (Ref. 73.G.923N)

Required to help with the research, content and writing of these programmes. Essential qualifications are a knowledge of film work and editing problems; the ability to work out story lines capable of visual illustration. Appropriate degree or knowledgeable interest in Natural History or Biology desirable. Based Bristol.

Research Assistant appointments will be made on contract for one year in the first instance.

Salary in the range £1,920-£2,130 p.a.

For all posts applicants must be prepared to make protracted overseas visits in rough conditions.

Write or telephone now for an application form (enclosing addressed foolscap envelope and quoting appropriate reference number) to

APPOINTMENTS DEPARTMENT, BBC,
LONDON W1A 1AA
Tel. 01-580 4468 ext. 4619

(1554)



Marine Biological Association of the United Kingdom

DIRECTOR

The Council of the Association will shortly proceed to the election of a Director of the Marine Biological Laboratory at Plymouth to take office on the retirement of Dr J. E. Smith, C.B.E., F.R.S., on 30th September, 1974. Those who wish their names to be considered are asked to inform the President

Sir Alan Hodgkin, O.M., P.R.S.,
Physiological Laboratory,
Downing Street, Cambridge CB2 3EG

not later than 19 December, 1973. The terms of the appointment will be arranged with the selected candidate.

(1535)

LINCOLN UNIVERSITY COLLEGE OF AGRICULTURE NEW ZEALAND

LECTURER/SENIOR LECTURER IN AGRICULTURAL METEOROLOGY

The Council of Lincoln College invites applications for appointment to the recently established position of Lecturer/Senior Lecturer in Agricultural Meteorology.

As this is the first College appointment in this field it is important that the appointee be able to communicate with agriculturalists and horticulturists as well as engineers and meteorologists.

Applicants should hold an appropriate degree and be capable of developing courses in Agricultural Meteorology and Climatology for degrees in Agriculture, Horticulture and Agricultural Engineering at undergraduate and postgraduate level.

Commencing salary according to qualifications and experience. The present salary scales for academic staff are: Lecturer \$NZ6,335-\$8,103; Senior Lecturer \$NZ8,249-\$9,723 (bar) \$10,019-\$10,606.

Removal expenses and fares of successful applicant will be reimbursed up to specified limits.

New Zealand Government Superannuation available. Conditions of appointment, giving further details of this position at Lincoln College, can be obtained from the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF, or from the Registrar of the University College.

Applications close on January 31, 1974. (1570)

UNIVERSITY OF THE WEST INDIES TRINIDAD

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN AGRICULTURAL ENGINEERING in the Department of Crop Science. Applicants must possess a postgraduate qualification in agricultural engineering, preferably with particular reference to its application to soil and water. Experience in tropical crop production and design of farm buildings is considered highly desirable, though not essential. Salary scales (under review): (a) £2,700-£4,200 per annum, (b) £1,850-£3,265 per annum. Child allowance. F.S.S.U. Family passages; triennial study leave.

Detailed applications (6 copies), including a curriculum vitae and naming 3 referees, should be sent as soon as possible to the Secretary, University of the West Indies, St. Augustine, Trinidad. Further particulars of the post will be sent to all applicants. (1561)

UNIVERSITY OF SYDNEY LECTURESHIP IN GEOPHYSICS

Applications from suitably qualified scientists are invited for the above-mentioned position in the Department of Geology and Geophysics. The Department offers a senior course in Exploration Geophysics and the appointee will be expected to lecture in this course. However, the Department is developing research in marine geophysics and preference will be given to applicants with experience in this field. Applicants should be prepared to take up duties early in 1974.

The position advertised is permanent but in appropriate cases an initial three-year appointment may be made with possibility thereafter of permanency or in certain cases return fares.

Salary: \$A8,698-\$A11,982 p.a.

Applications, including curriculum vitae, list of publications and the names of three referees, by January 18, 1974, to the Registrar, University of Sydney, N.S.W. 2006, Australia, from whom further information is available. Information also available from Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF. (1627)

UNIVERSITY OF ADELAIDE POSTDOCTORAL FELLOW IN MARINE PLANT BIOLOGY

Applications are invited for the above-mentioned appointment in the Department of Botany, to undertake a study of the effect of sewage effluent outfalls on marine plants (seagrasses and marine algae) within St Vincent Gulf, near Adelaide, South Australia. The appointment which is financed by a grant from the Australian Research Grants Committee, is available for a period of two years from January 1, 1974, with possible extensions for a third year.

Applicants should have completed a doctoral degree in some aspect of marine ecology, and should be familiar with marine plants and their reproduction, as well as instruments used in environmental assessment. Scuba experience is essential.

Salary scale: \$A6,967-353(4)-\$8,379.

Application in duplicate, giving particulars of age, qualifications (including dates obtained) and the names and addresses of two referees, should be sent to the Registrar, The University of Adelaide, GPO Box 498, Adelaide, South Australia 5001, as soon as possible, and no later than December 31, 1973.

Further enquiries should be addressed to Dr H. B. S. Womersley, Department of Botany, The University of Adelaide. (1628)

Senior Animal Technician

We have an opening, with excellent prospects of advancement, for a Senior Animal Technician at our new Pharmaceutical Research Centre at Milton Keynes.

Candidates should have experience of the handling and care of experimental animals including dogs, and will have the opportunity to make a real contribution to our research programme. Candidates should also be Fellows or Associates of the Institute of Animal Technicians.

Pharmacologist or Veterinary Surgeon

To assist in the design and execution of experiments related to the pharmacokinetics of novel drugs, we require an experienced Pharmacologist or Veterinary Surgeon. The successful applicant should have demonstrated practical skills with experimental laboratory animals, including dogs, and should have the capability of developing his own lines of research related to furthering the understanding of the mechanism of action of new drugs.

Autoradiography

We are seeking a Senior Scientist to lead a small team to design and carry out Autoradiography studies as part of our pharmacokinetic programme on drugs under development at our new Research Laboratories at Milton Keynes.

The person we seek will have experience in wholebody autoradiography and should be familiar with histological techniques. He, or she, should be capable of appreciating and developing the potentialities of autoradiography, particularly in its application to dynamics of pharmaceuticals.

Attractive salaries will be offered. The company also operates a merit bonus scheme, a contributory pension scheme and free membership for employees and dependants of the PPP Health Scheme. Assistance with house removal may also be available if required.

Would candidates, in the first instance, please write with fullest possible details to:

Personnel Officer,
Pharmaceutical Division,
Hoechst UK Limited,
Hoechst House,
Salisbury Road,
Hounslow, Middx.
Tel: 01-570 7712 ext. 3082

(1542)



STERLING-WINTHROP

GROUP

Sterling-Winthrop Group Medical Services is comprised of four departments which offer a medical and technical information service to all divisions within the Group. Sterling-Winthrop Group Ltd. is mainly comprised of several pharmaceutical companies concerned with the production and selling of ethical and over-the-counter medicines and household products. Conditions of service include a 36½ hour week, finishing at 4.00 p.m. on Fridays, a subsidised restaurant, 3 weeks' holiday increasing to 4 weeks' after one year's service, a sports and social club, and a contributory pension scheme. We now have two vacancies:

Technical Translator

Translations Department

A recent graduate with French to Honours Degree standard and German subsidiary is needed. Knowledge of a Scandinavian language and/or Spanish and/or Italian is a definite advantage. Duties will involve translation into English of medical and pharmacological reports and a wide variety of other material such as is required by an international pharmaceutical company. Training will be given to develop medical knowledge and terminology.

Medical Information Scientist

Technical Documentation Department

This small but vital department is responsible for the monitoring and evaluation of medical information relating to the development, marketing and promotion of the Group's ethical and proprietary products. Duties are varied and interesting including answering of enquiries and preparation of technical reports. Applicants should recently have obtained a degree or equivalent in a biological science. Previous experience in information work could be useful but is not essential.

Write for an application form and further details to:

Mrs. Hazel R. Lane, B.Sc., F.I.S., D.M.S., Controller, Group Medical Services,
Sterling-Winthrop Group Ltd., Winthrop House, Surbiton-on-Thames, Surrey

WINTHROP

(1602)

Glaxo Holdings Limited

Young Science Graduate *to work as a* Registration Officer

in the New Product Services Division based in Islington. The work involves the registration of Company products in specified overseas countries in which Glaxo Holdings Ltd. has a commercial interest. This entails the preparation of appropriate documents, editing submissions from within the Company before transmitting them overseas, dealing with queries and raising arguments in support of our submissions for presentation to overseas registration authorities, etc.

Applicants of either sex should hold a degree, preferably in the physical or biological sciences, and be within the age range 20-25 years. The Company offers full training, a salary in the range £1680-£1800 p.a. plus an opportunity to participate in the Company's profits. Fringe benefits are those which would be expected of a Company of international size.

Please write to or 'phone for an application form: Miss D. Packman, Personnel Department, Glaxo Holdings Ltd., Graham Street, London, N1 8JZ. Tel: 01-253 3060.

(1579)

UNIVERSITY OF LEICESTER DEPARTMENT OF PHYSIOLOGY SENIOR LECTURER

Applications are invited for the post of SENIOR LECTURER in the Department of Physiology (Head of Department, Professor R. Whittam, F.R.S.). Experience and an interest in teaching medical students are essential. Preference will be given to holders of a medical qualification, but other suitably qualified applicants will be seriously considered. There are excellent research facilities.

Initial salary, dependent on qualifications and experience, within the scale £4,368 to £5,496 a year, with F.S.S.U. membership.

Further particulars from the Registrar, to whom applications should be sent by December 11. (1423)

ARC ANIMAL BREEDING RESEARCH ORGANISATION

A vacancy arises of a research post concerned with studies of genetic control of mineral metabolism and of variation in production of ruminants. The work is relevant to animal breeding, nutrition and health. Candidates must have a good honours degree, with preferably postgraduate experience, a statistical aptitude and experience in data analysis. Appointment will be in the S.O./S.S.O. range (£1,318-£3,640) with FSSU.

Applications, with curriculum vitae and names of two referees, to the Secretary, ARC Animal Breeding Research Organisation, West Mains Road, Edinburgh EH9 3JQ. (1548)

UNIVERSITY COLLEGE CARDIFF

Applications are invited for the following vacancy:

POSTDOCTORAL FELLOW in the DEPARTMENT OF BIOCHEMISTRY

Salary Range: £1,764 × 159 × 156—£2,079; Duties to commence January 1, 1974, or as soon as possible thereafter. Closing date for applications December 10, 1973.

Applications, together with the names and addresses of two referees, should be forwarded to The Registrar, University College, P.O. Box 78, Cardiff, CF1 1XL, from whom further particulars will be available. Please quote 0941. (1544)

THE PUBLIC HEALTH LABORATORY SERVICE

requires

A SCIENTIST

to work at the MICROBIOLOGICAL RESEARCH ESTABLISHMENT, Porton Down, Salisbury, Wilts, to assist in an investigation of cell culture techniques for diagnosis of viral diseases.

The Appointment will be for 2 years in the first instance, subject to N.H.S. conditions of service and within the scale £1,278 to £1,980 (salary scale under review).

Apply with curriculum vitae to the Director, Microbiological Research Establishment by November 30, 1973. (1637)

QUEEN MARY COLLEGE UNIVERSITY OF LONDON

THEORETICAL PHYSICS

Applications are invited for a LECTURESHIP tenable from October 1, 1974. Preference will be given to candidates with interests in elementary particles or field theory. Salary scale £1,929-£4,548 p.a. plus £162 London Allowance. FSSU membership.

Applications are also invited for a RESEARCH FELLOWSHIP tenable from the same date, from candidates with interests in elementary particles or field theory. Salary scale £1,929-£2,553 p.a. plus £162 London Allowance.

Application forms available from The Registrar (N), Queen Mary College, Mile End Road, London E1 4NS, to be returned by January 7, 1974. Candidates overseas should ask their referees to write directly. (1534)

UNIVERSITY OF DURHAM DEPARTMENT OF PHYSICS

Applications are invited for the post of SENIOR DEMONSTRATOR in the Department of Physics from January 1, 1974, for two years in the first instance with possible renewal for a third and final year. The Demonstrator will be expected to carry out research in one of the following fields: Cosmic Rays, High Energy Nuclear Physics, Magnetism, Nuclear Instrumentation, Optical Astronomy.

The salary will be on the scale £1,719-£2,613 per annum with FSSU benefits.

Applications (3 copies) including the names and addresses of three referees should be sent by November 26, 1973, to the Registrar and Secretary, Science Laboratories, South Road, Durham DH1 3LE, from whom further particulars may be obtained. (1530)

UNIVERSITY OF MALAWI

BUNDA COLLEGE OF AGRICULTURE

Applications are invited for LECTURESHIP IN STATISTICS/MATHEMATICS, tenable as soon as possible. Applicants should have a degree in Statistics or equivalent qualifications or experience. The major responsibility will be to teach statistics to Degree and Diploma students. The post could be filled by a biometician or a statistician with an interest in teaching Mathematics. In the latter case, there would be an opportunity to teach Mathematics at both diploma and degree levels. Salary scale (including expatriate addition): £1,340-£2,250 p.a. plus either a University addition of £360 p.a. (taxable in Malawi) or supplementation (normally tax free) in appropriate case by the British Government, in range £600-£850 p.a. (if married) or £300-£550 p.a. (if single). The British Government may also provide children's education allowances and holiday visit passages. Gratuity: superannuation scheme transferable with FSSU; family passages; various allowances; biennial overseas leave; housing.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail, not later than December 17, 1973, to the Registrar, University of Malawi, University Office, PO Box 278, Zomba, Malawi. Applicants resident in UK should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London, W1P 0DT. Further particulars may be obtained from either address. (1635)

UNIVERSITY OF OXFORD

There will be a vacancy for a POSTDOCTORAL BIOCHEMIST or MICROBIOLOGIST to work on bacterial sporulation. The appointment which will be for one year in the first instance, at an initial stipend of £1,821, may be extended for a further period of two years and there is provision for FSSU or its equivalent.

Applications, which should include relevant details and the names of two referees, should be sent before February 1, 1974, to Professor J. Mandelstam, Microbiology Unit, Department of Biochemistry, South Parks Road, Oxford. (1555)

UNIVERSITY OF
THE WITWATERSRAND
JOHANNESBURG, SOUTH AFRICASENIOR LECTURER/LECTURER
IN ZOOLOGY

Applications are invited for appointment to the above vacancy in the Department of Zoology. Duties are to be assumed as soon as possible.

Salary will be in the following ranges:

Senior Lecturer: R7,245-R9,315 (£4,330-£5,635 approx.);

Lecturer: R5,520-R7,935 (£3,350-£4,800 approx.).

The initial salary will be determined according to qualifications and experience. Benefits include an annual bonus, pension and medical aid facilities, and a housing subsidy, if eligible.

Intending applicants should obtain the information sheet relating to this post from the Registrar, University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, South Africa with whom applications should be lodged not later than December 31, 1973. The information sheet may also be obtained from the London Representative, University of the Witwatersrand, Chichester House, 278 High Holborn, London WC1, with whom a copy of the application should be lodged. (1568)

UNIVERSITY OF IBADAN
NIGERIA

Applications are invited for LECTURESHIP IN GENETICS IN DEPARTMENT OF AGRICULTURAL BIOLOGY. Applicants should have a good background in Botany, Zoology or Applied Biology and postgraduate qualifications and experience in Genetics, Cytogenetics or Plant Breeding. Relevant teaching, research and curriculum development experience in a university will be an advantage as appointee will be expected to take an active part in teaching in both the undergraduate honours and postgraduate schools and in an integrated research programme in crop improvement and crop protection aspects of Agricultural Biology. Salary scale: N2,760-N4,830 p.a. (£1 sterling=N1.59.) The British Expatriates Supplementation Scheme is unlikely to be applied to this appointment. FSSU. Family passages; various allowances; regular overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail not later than December 14, 1973, to the Registrar, University of Ibadan, Ibadan, Nigeria. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (1571)

Department of Trade & Industry
Warren Spring Laboratory, Stevenage

Applied Rheologist

- Fundamental work on rheology and instrumentation to measure complex material properties ■ Application to industrial operations.
- ☐ Experience in the rheology of non-Newtonian fluids, slurries and pastes
- ☐ Ref: SA/11/MF.

Chemist/Physicist/
Engineer

- Install and operate air pollution monitoring equipment ■ Carry out quality control ■ Analyse and interpret data.
- ☐ Ref: SA/13/MF.
- ☐ For both posts, appointment as Scientific Officer ☐ Degree/HND/HNC in appropriate subject.

Chemist/Physicist

- X-ray powder diffraction work - phase analysis and characterisation of catalysts ■ Equipment partly computer controlled.
- ☐ Appointment as Higher Scientific Officer or Scientific Officer ☐ Degree/HND/HNC in a physical science ☐ Experience of X-ray diffraction procedures and in computing an advantage ☐ Ref: SA/12/MF.

Salary: HSO £2076-£2667, SO £1318-£2177.

Age: HSO under 30, SO under 27.

For HSO appointments, candidates must have at least 2 years relevant post-graduate experience.

- ☐ Application forms (for return by 7 December 1973) from The Director, Warren Spring Laboratory, Elder Way, Stevenage, Herts.

**Science
group**
CIVIL SERVICE

(1603)

WELSH OFFICE — Y SWYDDFA GYMREIG

Scientific Adviser
Health Services

£5550

This is a new appointment in Cardiff with overall responsibility for improving the effectiveness of scientific and technical aspects of the reorganised health services in Wales, and for advising on the implementation in Wales of the Zuckerman report.

Main duties will be: to interpret and contribute to policy; liaise with the DHSS and maintain two-way links with area health authorities and hospitals; advise on scientific services and staffing in the health service; plan vocational education and training of scientific and technical staff at all levels; some liaison on purchasing arrangements for scientific and technical equipment including questions of standardisation and variety reduction.

This key post calls for candidates, probably from 35 to 50 who hold a 1st or 2nd class honours degree, or an equivalent qualification, in a relevant subject. Success as an administrator and communicator essential.

Starting salary as shown. Annual increments to £6460. Non-contributory pension scheme. Promotion opportunities not confined to the Welsh Office.

Full details of this appointment may be obtained by writing to the Civil Service Commission, Alencon Link, Basingstoke, Hants., RG21 1JB, or by telephoning BASINGSTOKE 29222 ext. 500 or LONDON 01-839 1992 (24-hour answering service), quoting S/8440/U.

Closing date 6 December 1973.

(1597)

Research Assistants

Beecham Research Laboratories, Medicinal Research Centre, Harlow will shortly open a new purpose-built toxicology block which will considerably increase facilities for toxicological and drug safety assessment.

This expansion has created openings for technicians at all levels who are keen to do an important job well and to develop their practical skills and theoretical knowledge.

Animal Studies

We have a senior opening for someone with experience in drug safety and toxicology procedures in a pharmaceutical or university laboratory. Other essentials are experience handling experimental animals and the ability to lead junior staff.

We also have a number of junior posts for young men and women (aged 18-25) who have a minimum ONC or 5 'O' level qualifications—the latter to include Biology, Chemistry and Maths. Willingness to work with experimental animals is essential.

Haematology

This is a trainee post for someone with at least 5 'O' levels including Biology and Maths or an ONC. No previous experience is required and training will be given in haematological techniques. Age 17-20.

Clinical Chemistry

We have two senior vacancies for those with experience of clinical chemistry techniques, which could have been gained in either a pharmaceutical laboratory studying drug safety and toxicology or in a hospital pathology department. Age 20-30.

There are also more junior appointments for those aged 17-25 who have a minimum qualification of ONC or 5 'O' levels—the latter to include Chemistry, Physics and Maths.

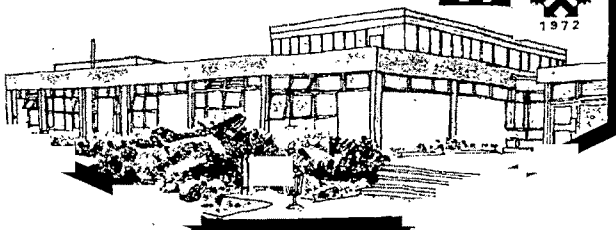
Histology

We have openings for senior technicians to share in the interesting and varied work of the Pathology section. Experience in general histological techniques is essential and this could have been gained in a pharmaceutical company or in a hospital pathology laboratory. Candidates are likely to possess an HNC or AILMT.

Starting salaries will be competitive and there are the usual fringe benefits associated with a large and expanding company. The Medicinal Research Centre is located near the Herts/Essex border and combines the facilities of a new town with proximity to London and pleasant surrounding countryside.

Please write, outlining your career to date, to
John Atkinson, Personnel Officer,
Beecham Research Laboratories,
Fourth Avenue, The Pinnacles,
Harlow, Essex.

(1547)



THE QUEEN'S UNIVERSITY OF BELFAST

Lectureship in Physiology

Applications are invited for a Lectureship in the Department of Physiology from January 1, 1974, or such other date as may be arranged. The successful applicant should have had experience in using histological techniques for research purposes and will assist in the teaching of histology to medical, dental and science students. The salary will be in the range £2,553-£4,548 but in certain circumstances may rise to £5,496. If medically qualified, the successful applicant may be paid an additional salary on a sessional basis by the Eastern Health and Social Services Board for hospital services undertaken over and above University duties. Both salaries carry contributory pension rights under the FSSU. The initial placing will depend on qualifications and experience.

Applications should be received by December 3, 1973. Further particulars may be obtained from the Personnel Officer, The Queen's University of Belfast, BT7 1NN. (Please quote Ref. 73/N.) (1574)

UNIVERSITY OF DAR ES SALAAM TANZANIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN AGRICULTURAL BOTANY in Department of Crop Science. Applicants should have a good honours degree in Botany, Agricultural Botany, or Agriculture, plus a higher degree and/or research experience in Botany or Agricultural Botany. Appointee will be required to teach Agricultural Botany, including Ecology and Agro-meteorology to undergraduates. He will also be expected to carry out research in his field of speciality and supervise postgraduates. Salary scales: (a) T£2,380-T£2,800 p.a. (b) T£1,898-T£2,318 p.a. (T£1=£1.18 sterling.) The British Government may supplement salary in range £550-£950 p.a. (sterling) for married appointee or £300-£650 p.a. (sterling) for single appointee and provide children's education allowances and holiday visit passages. FSSU. Family passages; biennial overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail not later than December 17, 1973, to the Chief Academic Officer, University of Dar es Salaam, P.O. Box 35091, Dar es Salaam, Tanzania. Applicants resident in UK should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (1633)

UNIVERSITY OF DAR ES SALAAM TANZANIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN SCIENCE EDUCATION (CHEMISTRY) in Department of Education. Applicants must have a good first degree in Science, including Chemistry. Preference will be given to those holding a higher degree. Appointee must have had some teaching experience at secondary level and must be acquainted with modern approaches to the teaching of Chemistry. He will be expected to teach Chemistry Methods to undergraduates; to conduct research in his area of specialisation; to assist with seminars in the more general areas of education and to participate in teaching practice supervision. Salary scales: (a) T£2,380-T£2,800 p.a. (b) T£1,898-T£2,318 p.a. (T£1=£1.18 sterling.) The British Government may supplement salary in range £550-£950 p.a. (sterling) for married appointee or £300-£650 p.a. (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. FSSU. Family passages; biennial overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than December 17, 1973, to the Chief Academic Officer, University of Dar es Salaam, P.O. Box 35091, Dar es Salaam, Tanzania. Applicants resident in UK should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of this appointment may be obtained from either address. (1634)

UNIVERSITY COLLEGE OF WALES
WELSH PLANT BREEDING STATION
APPOINTMENT OF
LIAISON OFFICER

Applications are invited from suitably qualified and experienced persons for a post as member of the Liaison Unit at the Station.

The salary range is £3,472 to £4,575 per annum and the commencing salary will be determined in the light of the successful applicant's qualifications and experience. The post is superannuated under FSSU.

The appointment is one of high responsibility and the successful applicant will be expected to undertake a wide range of duties associated with communicating the findings of research. It is expected that the successful candidate will have a scientific training and/or experience in the Public Relations field, with practical knowledge of the agricultural industry.

Full details may be obtained from the Secretary, Welsh Plant Breeding Station, Plas Gogerddan, Aberystwyth, Cards. SY23 3EB, to whom applications, together with the names of two referees, should be made by letter on or before November 30, 1973. (1565)

AGRICULTURAL RESEARCH
COUNCIL

has a vacancy for an ENTOMOLOGIST or a BIOLOGIST with entomological experience to take charge of the insectary in the Unit of Invertebrate Chemistry and Physiology at the University of Sussex. The successful applicant will be expected to be responsible for rearing insects for hormone bioassay, toxicity testing and biochemical research. Two full-time assistants are provided.

Appointment will be made in the Scientific Officer (£1,318-£2,177 p.a.) or Higher Scientific Officer (£2,076-£2,667 p.a.) grade, depending on qualifications and experience. Superannuation, with allowance to off-set contributions.

Minimum qualifications: pass degree, HNC or equivalent. At least five years' post-qualifying experience is required for appointment to the higher grade.

Preference will be given to candidates with experience of rearing insects for experimental purposes.

Applications should be made in writing to:

The Secretary,
ARC Unit of Invertebrate Chemistry and
Physiology,
The University of Sussex,
Falmer, Brighton, Sussex,
BN1 9QJ. (1566)

McMASTER UNIVERSITY
VIROLOGIST

A position is available for a Virologist at the Assistant or Associate Professor level. The appointee will be part of a viral oncology group being formed at McMaster University as well as a member of the Department of Biology. His/her research interests should be the molecular biology and/or genetics of animal viruses. His/her primary responsibility will be research and supervision of graduate students.

Applicants should send their curricula vitae and the names of three referees to the Chairman, Department of Biology, McMaster University, Hamilton, Ontario L8S 4K1, Canada, to arrive no later than January 15, 1974. (1581)

CAVENDISH MEDICAL CENTRE

A vacancy exists in the above Health Screening Centre for a CLINICAL BIOCHEMIST. This is an interesting post with good working conditions. Salary negotiable, commensurate with experience.

Applications to Mrs Payne, 99 New Cavendish Street, London W1. (1529)

UNIVERSITY OF STRATHCLYDE
DEPARTMENT OF APPLIED MICROBIOLOGY
TECHNICIAN—Grade 5

required for a period of two years, to work on a project concerned with the study of genetic changes in yeast during continuous culture. This work is supported by a SRC research grant. Candidates should have H.N.C. or degree, or equivalent in microbiology or related sciences.

Salary scale: Technician Grade 5, £2,007 to £2,382 per annum.

Applications in writing, quoting reference AM.55, giving details of age, experience and qualifications to The Personnel Officer, University of Strathclyde, Royal College Building, 204 George Street, Glasgow G1 1XW. (1600)

MEDICAL RESEARCH COUNCIL
JUNIOR TECHNICAL OFFICER

A Junior Technical Officer is required to assist a scientist with research in nucleic acid and protein synthesis in mammalian cells. Applicants should have a degree or H.N.C. in Biochemistry, Chemistry and Biology. Salary will depend upon age and experience on a scale rising to £2,073.

Applications in writing to the Administrative Officer, Clinical and Population Cytogenetics Unit, Western General Hospital, Crewe Road, Edinburgh 4, by November 30, 1973. (1601)

CSIRO
AUSTRALIA

DIVISION OF ANIMAL PHYSIOLOGY, PROSPECT, N.S.W.

RESEARCH SCIENTIST

FIELD:

ENDOCRINOLOGY

GENERAL. The Ian Clunies Ross Animal Research Laboratory is the headquarters of the Division of Animal Physiology of the Commonwealth Scientific and Industrial Research Organization, and is situated at Prospect, 20 miles west of Sydney, N.S.W. The Laboratory has a total staff of 150, including 55 professional scientists. Past and current research of the Laboratory includes work on endocrinology, nutrition, reproduction and lipid metabolism.

The Laboratory is continuing a programme of research on endocrinology in relation to growth and nutrition. An endocrinologist is required to collaborate with other endocrinologists and nutritionists on this programme of hormonal regulation of production in domestic animals.

DUTIES. To conduct research into the control of hormone secretion by diet and hormonal regulation of protein metabolism, fat metabolism, appetite, body growth, or wool growth.

QUALIFICATIONS. A Ph.D. degree or equivalent qualifications supported by demonstrable research ability. Experience in endocrinology related to steroids, polypeptide hormones or prostaglandins and the immunoassay of hormones would be an advantage.

SALARY. The appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A8,489-\$A12,932 p.a. An outstanding applicant may be offered appointment at a higher level.

TENURE. Either an indefinite or a fixed term appointment may be negotiated. An indefinite appointment carries Australian Government Superannuation benefits.

Applications, stating full personal and professional details, the names of at least two professional referees, and quoting Reference Number 245/561 should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64-78 Kingsway, London, WC2B 6BD.
by the 14th December, 1973.

Applications in U.S.A. and Canada should be sent to:

The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
Washington, D.C. 20036, U.S.A.

(1583)

MONASH UNIVERSITY
MELBOURNE, AUSTRALIA
CHAIR IN ZOOLOGY

A second professorship in Zoology has recently been established. Applications are invited from zoologists whose research interests coincide with one of the following established areas in the department: ecology, comparative physiology, developmental biology, and behaviour. The Department of Zoology comprises fourteen academic staff with supporting technical officers and is well equipped to conduct research and teaching in the above-mentioned fields. It is expected the appointee will assume duties in late 1974 or early 1975.

Further information concerning the Department is available from the Chairman, Professor J. W. Warren, in the University.

Salary: \$A19,102 per annum. Superannuation is based on an endowment assurance scheme, the employee and employer contributing 5% and 10% respectively.

Information on application procedure and further particulars may be obtained from the Academic Registrar, Monash University, Clayton, Victoria 3168, Australia, or the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF.

Applications should reach the Academic Registrar not later than January 11, 1974. The Council reserves the right to make no appointment or to appoint by invitation at any stage. (1624)

NATIONAL INSTITUTE FOR
RESEARCH IN DAIRYING
(UNIVERSITY OF READING)
BACTERIOLOGY DEPARTMENT

A SUPERVISOR is required for a section responsible for preparation of bacteriological media. Applicants should have had sound training in chemistry or bacteriology.

An appropriate degree, H.N.D., H.N.C., or equivalent is required. The appointment will be in the Scientific Officer grade within a scale of £1,318 to £2,177 per annum according to qualifications and experience. Superannuation, with an allowance to offset contributions. Apply on forms obtainable from the Secretary, National Institute for Research in Dairying, Shinfield, Reading RG2 9AT. Quote reference 73/46. (1471)

CHAIRMAN—DEPARTMENT OF
ANATOMY

Columbia University, College of Physicians and Surgeons, an equal opportunity employer, is seeking an individual as Chairman of Anatomy Department. Should be qualified medical scientist and experienced medical educator.

Send curriculum vitae to: Myron Winick, M.D., Chairman, Search Committee, Institute of Human Nutrition, 511 West 166th Street, New York, New York 10032. (1289)



VRIJE UNIVERSITEIT AMSTERDAM

Applications are invited for the position of

hydrologist

in the Hydrology Program of the Institute of Earth Sciences. Appointment commences January 1st '74. Candidates should be experienced hydrologists with a math.-physics background, preferably Ph.D., Dutch nationality preferred.

Duties:

teaching of surface water hydrology at graduate level in the laboratory and in the field in co-operation with the present faculty group, some additional undergraduate teaching in hydrology.

Submit inquiries to Dr. G. B. Engelen, Chairman Hydrology Program, Institute of Earth Sciences, 1085 De Boelelaan, Amsterdam, Netherlands.

Candidates are expected to be in agreement with the Christian principles of the Free University.

Applications should be sent to Hoofdafdeling Personeelszaken, P.O. Box 7161, Amsterdam.

(1541)



UNIVERSITY COLLEGE OF NORTH WALES, BANGOR DEPARTMENT OF APPLIED ZOOLOGY RESEARCH ASSISTANT

Applications are invited for the post of Research Assistant in the above Department, to work under Dr J. M. Cherrett on the development of baits against tropical leaf-cutting ants. The main work will involve behavioural, chemical and developmental studies on laboratory colonies.

Applicants should have a good honours degree in Zoology, or in a closely related subject, and preference will be given to applicants with research experience in the general field of animal behaviour.

Starting salary will be £1,326 per annum and the initial appointment will be for one year commencing on January 1, 1974, with a possibility of renewal by mutual consent.

Applications (two copies) with full details of age, qualifications and experience, together with the names and addresses of two referees, should be sent not later than November 30, 1973, to the Secretary and Registrar, University College of North Wales, Bangor, from whom further particulars may be obtained.

(1531)

BEHAVIOURAL BIOLOGIST

The University of Chicago's Department of Biology invites applications for a faculty appointment in the area of behavioural biology. The University is an equal opportunity employer. Selection will be made on the basis of excellence and vigour in research and teaching. Applicants should forward the following material by December 31, 1973: (i) a curriculum vitae, including bibliography and reprints; (ii) names, addresses and telephone numbers of five references, and (iii) a summary, not to exceed two typed pages, of your current research plans and long-term goals. Material should be sent to Professor Hewson Swift, Chairman, Department of Biology, The University of Chicago, Chicago, Illinois 60637.

(1562)

HAMPSHIRE RIVER AUTHORITY ASSISTANT FISHERIES OFFICER DEPARTMENT OF TECHNICAL SERVICES £2,235-£2,820 p.a.

This is a new post to assist the Fisheries Officer in the operation of the Authority's Fishery functions. The successful applicant will be particularly responsible for developing a fisheries sampling programme to monitor the various fisheries. The Rivers Test and Itchen, important game fishing rivers, are contained within the Authority's area.

Applicants should hold a degree in a biological subject, preferably zoology, with some specialist training or experience in freshwater fisheries. The commencing salary will be related to qualifications and experience.

Further details and application forms are available from the Chief Administrative Officer, Hampshire River Authority, Eastleigh House, Market Street, Eastleigh, Telephone Eastleigh 7444, extension 48. Closing date for applications is December 10. Please quote reference SE2363/U.

(1546)

UNIVERSITY OF NEW SOUTH WALES SCHOOL OF MATHEMATICS, LECTURER

Salary: \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

In the field of mathematical statistics. High academic qualifications required, together with research experience in statistics and/or probability theory; teaching experience in these areas advantageous.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London, WC1H 0PF. Applications close in Australia and London on December 14, 1973.

(1551)

UNIVERSITY OF MANCHESTER INSTITUTE OF SCIENCE AND TECHNOLOGY

TECHNICIAN (GRADE 5)

(REF.: CH/453/AI)

required in the Department of Chemistry to join a team engaged on interesting work in organic chemistry. A knowledge of chemical theory to H.N.C. level is desirable, but the requirements of the post place greater emphasis on practical ability in preparative chemistry. The post will give the successful candidate the opportunity to learn special techniques used in the work, and to further his theoretical background.

Salary within the scale £2,007 to £2,382 per annum. Requests for application forms, quoting reference number, should be addressed to the Registrar, U.M.I.S.T., Sackville Street, Manchester M60 1QD, to be returned no later than November 28, 1973.

(1592)

CHELSEA COLLEGE UNIVERSITY OF LONDON

TECHNICIAN GRADE 2A required in the Microbiology Section of the Biological Sciences Group. Duties will include assisting in the preparation of media, reagents and cultures for undergraduate teaching and postgraduate research activities. Previous experience in Microbiology (bacteriology, mycology, virology) is required. Salary scale: £1,552 to £1,822 per annum (including London Allowance).

Application forms from Mr K. Harris (N), Department of Applied Biology, Chelsea College, Hortensia Road, London SW10 0QX.

(1590)

UNIVERSITY OF NAIROBI KENYA

Applications are invited for the following posts in the FACULTY OF VETERINARY SCIENCE:

1. SENIOR LECTURER IN DEPARTMENT OF VETERINARY PATHOLOGY AND MICROBIOLOGY. Applicants should be Veterinarians with a Ph.D. in Pathology or equivalent backed by considerable experience in research or teaching in Veterinary Pathology or animal diseases. Appointee will be required to assume responsibilities for lecturing and practicals in general systematic pathology and disease description course for undergraduate veterinary students and participate in research, tuition of graduates and routine diagnosis.

2. LECTURER IN DEPARTMENT OF PUBLIC HEALTH, PHARMACOLOGY AND TOXICOLOGY. Applicants should be Veterinarians with postgraduate training of either a Masters degree or a Diploma in Meat and Food Hygiene. Experience in organisation and working in slaughter houses would be an advantage.

Salary scales: (a) K£2,256 to K£3,036 per annum; (b) K£1,500 to K£2,580 per annum (K£1=£1.18 sterling). The British Government may supplement salaries in range £450 to £950 per annum (sterling) for married appointees or £150 to £650 per annum (sterling) for single appointees (normally free of all tax) and provide children's education allowances and holiday visit passages. F.S.S.U. Family passages; various allowances.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail, not later than December 14, 1973, to the Registrar, University of Nairobi, P.O. Box 30197, Kenya. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of these appointments are obtainable from either address.

(1589)

BRITISH ANTARCTIC SURVEY SCIENTIFIC OFFICER

Applications are invited for the post of Biological Assistant to work in the Huntingdon/Cambridge area. The duties of the post may include:

- Operation of OHN analyser and bomb calorimeter.
- Operation of liquid scintillation counter.
- Preparation of histological sections, moss core sections and photomicrography.
- Analysis of microclimate records.
- Maintenance of cultures.
- Routine sorting and counting of samples.

QUALIFICATIONS

Candidates should be under 27 years of age with a degree or equivalent in a relevant subject.

SALARY SCALE

£1,318 to £2,177. Starting pay according to qualifications and relevant experience.

Application forms may be obtained from The British Antarctic Survey, 30 Gillingham Street, London SW1V 1HY.

Closing date: November 30, 1973.

NATURAL ENVIRONMENT RESEARCH COUNCIL

(1598)

TECHNICIAN

at

The Open University

The Materials Science and Engineering Mechanics Disciplines of the Faculty of Technology require a Technician to assist the staff of the Faculty in scientific research and laboratory work associated with television, visual aids and kits of experimental apparatus for students' use in their own homes.

Candidates are expected to have an ONC/HNC or equivalent qualification in metallurgy and/or mechanical engineering, with at least four years' experience. Candidates from allied engineering backgrounds will also be considered.

Salary, according to age, experience and qualifications, will be within the scale: £1,848-£2,163 per annum, with superannuation benefits.

Application forms and further particulars are available from **The Acting Personnel Manager, The Open University (EM2)**, P.O. Box 75, Walton Hall, Milton Keynes, MK7 6AL. Closing date: Friday, 30th November, 1973.

(1569)

THE UNIVERSITY OF LEEDS.

DEPARTMENT OF PLANT SCIENCES

TWO RESEARCH ASSISTANTS are required for a project to investigate the effects of nutrient and fertiliser salts on crop plants during the early stages of development, in relation to environmental variables. The posts would suit holders of degrees in botany, soil science or agricultural science, with an interest in crop nutrition or plant physiology. Salary on the scale £1,449 to £1,818.

Forms of application and further particulars from the Registrar, The University, Leeds LS2 9JT (please quote 41A/7/D). Closing date November 30, 1973. (1585)

NORTHERN REGIONAL HOSPITAL BOARD (SCOTLAND)

Applications are invited for the newly established post of BASIC GRADE BIOLOGIST (Graduate) in the Pathology Department of the Regional Hospital Board's Laboratories at Inverness. If possible prospective candidates should have special experience in cancer chemotherapy screening and/or tumour immunology. Salary in accordance with Whitley Council agreements.

Further particulars and forms of application are obtainable from the Senior Administrative Medical Officer, Northern Regional Hospital Board, Reay House, 17 Old Edinburgh Road, Inverness, with whom applications should be lodged by December 10, 1973. (1578)

A STATE REGISTERED SENIOR MEDICAL LABORATORY TECHNICIAN with F.I.M.L.T. and experience in bacteriology and interest in biochemistry is required for a new research laboratory for bacterial metabolism at Central Public Health Laboratory, Colindale Avenue, London, N.W.9. N.H.S. salary rates and conditions of service.—Applications to Public Health Laboratory Service Board, 24 Park Crescent, London W1N 4DA. (1580)

MEDICAL RESEARCH COUNCIL LABORATORY OF MOLECULAR BIOLOGY. A vacancy has arisen for a Postdoctoral Organic Chemist or Biochemist in a group working on the partial synthesis and folding properties of proteins. Two-year appointment in the first instance; stipend about £2,100 per annum.—Applications, giving details of age, qualifications and experience and the names of two referees to Dr. R. C. Sheppard, M.R.C. Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, as soon as possible. (1587)

LANCHESTER POLYTECHNIC

Coventry - Rugby

Applications are invited for the following posts:

FACULTY OF ENGINEERING

LECTURER GRADE II IN

Production Engineering

Economics for the Construction Industry

RESEARCH ASSOCIATE/ASSISTANT (2 POSTS) IN

Electrical, Mechanical, Production Control or Civil Engineering, Educational Technology

FACULTY OF APPLIED SCIENCE

PRINCIPAL LECTURER AND LECTURER GRADE II IN

Mathematics

SENIOR LECTURER/LECTURER GRADE II IN

Physics

LECTURER GRADE II IN

Operational Research

RESEARCH ASSOCIATE/ASSISTANT IN

Applied Numerical Analysis

Chemical Metallurgy (Corrosion Fatigue)

Salaries:

Principal Lecturer: £3581 - £3989 - £4499 p.a.

Senior Lecturer: £3291 - £3655 - £3928 p.a.

Lecturer Grade II: £2515 - £3243 p.a.

Research Associate: £1846 - £2008 p.a.

Research Assistant: £1360 - £1522 p.a.

In certain circumstances the commencing salary for the above posts may be above the minimum scale. The qualifications and experience for appointment are stated in Further Particulars, which are available with application forms, from Assistant Secretary (Personnel), Lanchester Polytechnic, Priory Street, Coventry CV1 5FB, (Telephone: 24166 Extension 392) returnable by 30 November 1973. (1576)

North East London Polytechnic

Technician T3—Geology

Applications are invited for the above post in the Department of Chemistry, based at our West Ham Precinct, Romford Road, London E.15. Duties will be in the field of GEOLOGY involving maintenance of collections, servicing the sections laboratory, class preparations and the preparation of samples and slides. Applicants should possess at least ONC/AIST level qualifications with preference given to candidates with experience in the Geology field. Knowledge of photography and general laboratory procedures an advantage. Salary on a scale ranging from £1521 to £1749 per annum inclusive. Please telephone our Staffing Office, 01-555.0811 ext. 31, ref. S/CF123 for an application form and return it by 29 November, 1973. (1622)

MEDICAL RESEARCH COUNCIL

RADIOBIOLOGY UNIT, HARWELL, BERKSHIRE

TECHNICAL ASSISTANT (BIOLOGIST) wanted. Excellent opportunity for (a) Young Graduate or (b) Holders of HNC to join a research group investigating genetic effects of radiation and other agents in small animals. Varied work involving animal genetics, cytogenetics, tissue culture etc. Salary according to age and qualifications. Fringe benefits include modern hostel accommodation for single men and women at a reasonable cost, excellent social facilities and proximity to Oxford.

Applications in writing to: The Administrator, Medical Research Council, Radiobiology Unit, Harwell, Berkshire. Reference MFL/32. (1613)

Graduate Biochemist/ Plant Physiologist

Shell Research Ltd., Sittingbourne, Kent, have a vacancy for a young graduate biochemist or plant physiologist in the Biochemistry and Plant Physiology Division of their Milstead Laboratory of Chemical Enzymology. You will participate in a study of the metabolism of hormones in plants and of the enzymes involved. There will be extensive use of radio isotope techniques. You will be expected to have knowledge of and experience in a variety of biochemical techniques. You should have a good Honours degree and an M.Sc. or Ph.D in Biochemistry or Plant Physiology. Chemistry post-graduates will also be considered if their studies have covered a substantial amount of plant biochemistry and enzymology. The level of appointment will depend on your background and experience; the salary will be competitive. Please write, giving details about your background and experience, to Shell Research Limited, Recruitment Division, PNEI/31, Shell Centre, London SE1 7NA.



(1636)

UNIVERSITY OF TORONTO DEPARTMENT OF PHYSICS

Applications are invited for a faculty position at the level of ASSISTANT PROFESSOR in the Department of Physics. Applicants should have a Ph.D. and research experience in solid earth physics. The solid earth physics group in the Department of Physics has an active and well supported research programme in geomagnetism, crustal seismology, tectonics and geochronology, and works in close co-operation with the Department of Geology. Appointment will be effective July 1, 1974.

Applicants should send curriculum vitae and names of three referees to: Professor D. J. Rowe, Department of Physics, University of Toronto, Toronto M5S 1A7, Ontario, Canada. (1439)

RICHMOND COLLEGE CITY UNIVERSITY OF NEW YORK DIVISION OF PURE AND APPLIED SCIENCES ENVIRONMENTAL SCIENCE

Applications are invited for a faculty position in geology, oceanography, or meteorology. The position involves active participation in the graduate Environmental Science programme and related upper-level undergraduate course offerings. A PhD in an appropriate field is required; rank depends on experience. Salary and benefits are among the highest in the U.S. Richmond College is an upper-division unit of C.U.N.Y. located on residential Staten Island, close to, but detached from, mid-town New York City.

Send résumé and references to Dr A. M. Levine, Division of Pure and Applied Sciences, Richmond College, 130 Stuyvesant Place, Staten Island, New York 10301, USA. (1556)

AGRICULTURAL RESEARCH COUNCIL INSTITUTE FOR RESEARCH ON ANIMAL DISEASES COMPTON, BERKSHIRE HELMINTHOLOGIST

Applications are invited from graduates with at least an upper second class honours degree and a minimum of two years' research experience for a vacant post in the Institute's Department of Parasitology. Preference may be given to a candidate who has obtained a Ph.D. degree. The successful candidate will be required to conduct research on nematodes of farm livestock and initially will be expected to study nematode/bacterial interactions.

The appointment will be in the H.S.O. (£2,076 to £2,667)-S.S.O. (£2,615 to £3,640) scales according to qualifications and experience, plus a 41 per cent allowance to offset F.S.S.U. superannuation contributions. Applications, accompanied by a curriculum vitae and the names and addresses of two referees, should be submitted to the Institute Secretary, citing vacancy No. 153, by November 30, 1973. (1496)

RESEARCH ASSISTANT WANTED

to join a small team working on problems of the relation between enzyme induction, nutrition, and cell injury by environmental chemicals. Biochemistry graduate preferred, but what the post requires most is interest and willingness to learn many techniques ranging from spectrophotometry to making diets. Salary: £1,400-£1,800 (Whitley Council scale).

Applicants write to: Dr A. McLean, Department of Experimental Pathology, UCH Medical School, University Street, London WC1, giving details of any experience and qualifications. (1559)

GRADUATE OR POSTDOCTORAL RESEARCH ASSISTANT

required for one year in the first instance, to work in the Department of Microbiology under the direction of Professor C. A. Mims on the pathogenesis of murine cytomegalovirus infection. Some postgraduate experience in virology and tissue culture desirable.

Initial salary in the range £1,569 to £2,550 according to qualifications and experience.

Applications, together with the names of two referees, to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, by December 15. (1593)

UNIVERSITY OF IBADAN NIGERIA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN DEPARTMENT OF VETERINARY MEDICINE AND SURGERY. Applicants should be holders of appropriate qualifications and possess some teaching and research experience. Salary scales: (a) N5,030 to N6,150 per annum; (b) N2,760 to N4,830 per annum (£1 sterling=N1.59). The British Government may supplement salaries in range £750 to £1,150 per annum (sterling) for married appointee of £250 to £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances; superannuation scheme; biennial overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than December 17, 1973, to the Registrar, University of Ibadan, Ibadan, Nigeria. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (1604)

CHELSEA COLLEGE UNIVERSITY OF LONDON

RESEARCH TECHNICIAN (TEMPORARY) GRADE 3 required to work on an Environmental Research Project in the Department of Applied Biology of the Biological Sciences Group. Experience of atomic absorption and spectrophotometry essential. Salary scale £1,825 to £2,095 per annum including London Allowance.

Application forms from Mr K. Harris (N), Department of Applied Biology, Chelsea College, Hortensia Road Annexe, London SW10 0QX. (1605)

UNIVERSITY OF ADELAIDE

Applications are invited for the following appointments:

LECTURER IN BOTANY from beginning of 1974, to teach at both undergraduate and postgraduate levels in ecology. Higher degree required. Field should be relevant to current environmental problems and might include plant ecology, general ecology (provided interests embrace plants) or related topics, such as phytoplankton and marine productivity or physiology of plants under stress. (15.12.73).

TEACHING FELLOW IN ORGANIC CHEMISTRY for 1974 from candidates with Ph.D. degrees; to be responsible for practical courses including course innovations and to undertake research with existing research groups, which enjoy modern facilities of high standard. (7.12.73).

Salary scales: Lecturer SA8,698-SA470 (1)-SA469 (6)-SA11,982; with superannuation on the F.S.S.U. basis; Teaching Fellow SA7,270-SA286 (3)-SA285 (2)-SA8,698; a non-superannuated and non-tenured appointment.

Further particulars about these posts and the conditions of appointment and other information sought will be supplied on request to the Registrar of the University, or to the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications should be sent in duplicate and giving the information listed in the Statement that will be supplied, to the Registrar, the University of Adelaide, North Terrace, Adelaide, South Australia, 5001. (1606)

RESEARCH SPECIALIST or FELLOW required immediately to carry out cellular biophysical research in the Laboratory of Biophysics, Department of Biological Sciences, University of Denver, Denver, Colorado 80210, USA, under the supervision of Professor G. B. David, from whom further particulars may be obtained. Experience in ultrastructural work, enzyme histochemistry or cell isolation techniques required. Bachelor's or Master's degree and adequate post-graduate experience needed. Exceptionally well equipped laboratory available. (1617)

UNIVERSITY OF MANCHESTER

Applications are invited for the post of **LABORATORY SUPERVISOR** in the Department of Physiology. The Department is housed in the new Medical School Building and has well equipped laboratories and workshops. Duties will include the recruitment and supervision of technical staff and the provision of a technical service covering both teaching and research. The successful candidate will also be required to advise the Head of Department on the use and purchase of equipment and apparatus and be responsible for the maintenance of expenditure records. Applicants should have an HNC or equivalent qualification and a minimum of 10 years' relevant experience preferably in a biological sciences background. Salary scale £2,817-£3,201 p.a.

Applications, giving full details of age, qualifications and experience together with the names of two persons to whom reference may be made should be sent as soon as possible to Professor S. Thomas, Department of Physiology, The University, Stopford Building, Manchester M13 9PT, from whom further particulars may be obtained. (1609)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS. AL5 2JQ

A **SCIENTIFIC OFFICER** is required to work at Broom's Barn Experimental Station on magnesium and other nutrients for arable crops.

The appointment will be for a period not exceeding four years, and there will be an opportunity for a suitably qualified appointee to register for a higher degree.

Qualifications—1st or 2nd class honours degree in appropriate agricultural science subject. Appointment in grade of Scientific Officer (£1,318 to £2,177 per annum) (under review). Starting salary according to age, qualifications and experience.

Applications to the Head of Broom's Barn Experimental Station, Higham, Bury St. Edmunds, by December 7, from whom further particulars may be obtained. (1620)

UNIVERSITY OF TORONTO
DEPARTMENT OF GEOGRAPHY

Applications are invited for a position in physical and biogeography, Department of Geography, St. George Campus, University of Toronto, beginning July 1, 1974. The successful candidate will be expected to develop and teach courses in natural environmental systems in close relationship with existing specialised courses in physical geography and resource management. The courses will be at both the introductory and more advanced levels. The candidate should have a Ph.D. in Geography or another appropriate field. Preference will be given to candidates with a demonstrated interest in ecosystems, both natural and man-modified. The rank will be either **ASSISTANT** or **ASSOCIATE PROFESSOR**.

A letter of application, with curriculum vitae and the names of three referees, should be sent to Professor J. Spelt, Chairman, Department of Geography, University of Toronto, Toronto M5S 1A1, Ontario. Applications should be submitted before February 15, 1974. (1616)

UNIVERSITY OF TORONTO
ASSISTANT PROFESSOR IN
BIOCHEMISTRY

Applications are invited for the position of Assistant Professor in the Department of Biochemistry, to take effect from July 1, 1974, or as soon thereafter as possible. The successful applicant will be required to take part in the teaching duties of the Department and develop his own research programme. The Department is involved in teaching undergraduates in the Faculties of Medicine, Dentistry, Arts and Science, and Nursing, as well as the Graduate School. The minimal salary for the position is \$14,300.

Applicants with suitable qualifications should send a curriculum vitae and the names and addresses of three referees, to Professor T. Hofmann, Department of Biochemistry, University of Toronto, Toronto, Canada M5S 1A8, to reach him not later than January 31, 1974. (1615)

THE MOTOR INDUSTRY RESEARCH
ASSOCIATION
MAN AND VIBRATION

An **ENGINEER/PHYSICIST** is required to join a small research team investigating the effects of road vehicle vibration on man.

Preference will be given to candidates with R&D experience, and in particular those experienced in the use of one or more of the following:

Electronic recording and analysing equipment
Statistical analysis techniques
Digital and analogue computing.

Qualifications: Degree or C.Eng.
The starting salary in the range £1,700-£3,200 will depend on qualifications and experience.

Apply in writing to MTP, Warrington, Cheshire.

CSIRO
AUSTRALIA

DIVISION OF PLANT INDUSTRY, CANBERRA, A.C.T.

RESEARCH SCIENTIST

FIELD:

PLANT/WATER RELATIONS

GENERAL. The Division of Plant Industry of the Commonwealth Scientific and Industrial Research Organization, with headquarters at Canberra, is conducting a comprehensive programme of crop and pasture research based on field and phytotron experiments in a number of disciplines including Agronomy, Nutrition, Physiology, Biochemistry, Genetics, Ecology, and Agricultural Systems. The Crop Adaptation Section is studying the response of a range of crops, including cereals and protein and oil seeds, to dryland conditions.

DUTIES. To conduct field and controlled environment studies on the physiological basis of adaptation to water stress in rain-fed crops.

QUALIFICATIONS. A Ph.D. degree or equivalent qualifications and demonstrable research ability.

SALARY. The appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A8,489-\$A12,932 p.a. An outstanding applicant may be offered appointment at a higher level.

TENURE. Either a fixed term or an indefinite appointment may be negotiated. An indefinite appointment carries Australian Government Superannuation benefits.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting Reference Number 130/1248, should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64-78 Kingsway, London, WC2B 6BD.

by the 14th December, 1973.

Applications in U.S.A. and Canada should be sent to:

The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, NW,
Washington, D.C. 20036, U.S.A.

(1582)

Newcastle Regional Hospital Board

REGIONAL MEDICAL PHYSICS
DEPARTMENT

Physicist (basic grade)

Applications are invited for the post of Physicist in the Cardiology Section of the Regional Medical Physics Department, Newcastle General Hospital. This Section is concerned with patient monitoring during surgery and intensive care, computer analysis of catheterisation data and applications of electronics to cardiology. Candidates should have a good honours degree as well as a keen interest in electronics. There may be opportunity for taking a higher degree.

Further information may be obtained from the Chief Physicist of the department (Newcastle 31577).

Salary £1,566 per annum rising by annual increments to £1,842 per annum at end of two years.

Applications to the Secretary, Newcastle Regional Hospital Board, Benfield Road, Walker Gate, Newcastle upon Tyne, NE6 4PY within three weeks.

(1581)

British Museum (Natural History)

Science Writer

The Museum is developing a new exhibition to present a modern view of natural history. A "science writer" is needed to prepare copy and caption material for use in the new exhibition as well as guide books and information leaflets relating to the displays.

The person appointed will also be responsible for writing expositions on recent advances in natural history, for sale to the general public.

All this writing will be done in conjunction with the scientific staff of the Museum.

Candidates should normally have a 1st or 2nd class honours degree in a scientific subject and have a broad knowledge of the biological sciences. They must offer evidence of a facility for presenting complex information in clear and attractive non-technical language without prejudicing its scientific accuracy. A lively interest in communication and modern natural history is required.

Appointment will be as Senior Scientific Officer (£2790-£3815), Higher Scientific Officer (£2251-£2842) or Scientific Officer (£1493-£2352), according to age, qualifications and experience.

For further information and an application form (to be returned by 7 December 1973), write to Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB or telephone Basingstoke 29222 ext. 500 or London 01-839 1992 (24 hour answering service). Please quote SB/11/DK.

(1557)

Senior Toxicology Technician

Smith Kline & French Laboratories Limited is an international leader in the pharmaceutical industry. The Research Institute at Welwyn Garden City is part of the European Research function.

A Senior Toxicology Technician is required to lead the animal studies team in the Toxicology Department which is concerned with the safety assessment of new compounds.

Minimum requirements are

experience with laboratory animals and the possession of a Home Office licence. H.N.C. or F.I.A.T. is preferred. This is a post which is particularly suitable for someone with an ability to organise.

As part of an international organisation the company offers an excellent range of benefits. Salary is negotiable dependent upon experience.

Please write, giving brief details of career to date to:

The Personnel Officer,
Smith Kline & French Laboratories Limited,
Mundells, Welwyn Garden City, Herts.

(1608)



ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS. AL5 2JQ

SCIENTIFIC OFFICER required to help head of department with research on physicochemical factors influencing the performance of pesticides, and on methods of improving pesticide use. At present the behaviour of systemic insecticides and fungicides in soil and their uptake by plants are being studied, but the future programme is expected to involve a range of problems including studies on uptake of chemicals by insects.

Minimum qualifications: pass degree, HNC or the equivalent, preferably with chemistry or agricultural chemistry as a main subject. Starting salary £1,318-£1,590 according to qualifications and experience, on scale to £2,177. Superannuation with allowance to offset contributions.

Applications, naming two referees and quoting reference 2042, to the Secretary by December 7, 1973. (1619)

ROWETT RESEARCH INSTITUTE

BUCKSBURN, ABERDEEN, AB2 9SB

SCIENTIFIC OFFICER

Applications are invited for a scientific post in the Department of Experimental Pathology. The successful candidate will be encouraged to undertake original work on toxic effects of dietary constituents in farm animals. A special interest in EM techniques and ultrastructural morphology, and ability to work with farm animals, are essential.

Salary scale is £1,318 per annum rising to £2,177 per annum. Candidates should have at least a good second class honours degree in science, and salary placing will be according to qualifications and post-graduate experience. The post is superannuated with a non-pensionable allowance to offset contributions.

Applications, containing full biographical details and names and addresses of two referees, should reach the Secretary of the Institute before December 14. Further particulars of the duties of the post can be had on application. (1611)

QUEENSLAND INSTITUTE OF TECHNOLOGY

QUOTE: V. 159.73

SENIOR TUTOR IN ORGANIC CHEMISTRY

Applications are invited for the above position within the Department of Chemistry. Preference will be given to candidates who have a higher degree and/or industrial experience. It would be advantageous for applicants to have some experience in food science or applied biochemistry. The successful applicant will carry out demonstrating, tutorial and some lecturing duties and preferably be available before August, 1974.

Salary range: \$6,969-\$7,855 per annum. Further particulars may be obtained from the Registrar.

Applications, including curriculum vitae and the names and addresses of two referees, by December 31, 1973, to: The Registrar, Queensland Institute of Technology, P.O. Box 246, North Quay, Queensland 4000, Australia. (1610)

RESEARCH ASSOCIATESHIP in the Laboratory of Biophysics, Department of Biological Sciences, University of Denver, Denver, Colorado 80210, USA, to carry out research in ultrastructural chemistry under the supervision of Professor G. B. David, from whom further particulars may be obtained. The appointment, available immediately, is for 1 calendar year, renewable. Minimum qualifications include a doctoral degree and appropriate research experience. Exceptionally well equipped laboratories available. (1618)

UNIVERSITY OF EDINBURGH

DEPARTMENT OF GENETICS

POSTDOCTORAL RESEARCH FELLOW

A vacancy exists for a Postdoctoral Research Fellow in a programme concerned with mutation induction in continuous cultures of micro-organisms. Experience in genetical work on micro-organisms required; biochemical experience desirable.

Salary on scale £1,929-£2,388. Applications (in writing), together with curriculum vitae and the names of two referees, should be sent to the Secretary to the University, Old College, South Bridge, Edinburgh EH8 9YL, not later than December 20, 1973. Please quote reference 5081. (1630)

THE ROYAL VETERINARY COLLEGE LONDON

DEPARTMENT OF PATHOLOGY

Applications are invited for the post of VIROLOGIST to assist in a research project on cytomegalovirus infection of pigs, financed by the Agricultural Research Council.

The post will be particularly attractive to those interested in persistent infections by herpes viruses; good facilities and germ-free piglets are available. There would be opportunities to study for a higher degree. A veterinary qualification would be an advantage but is not essential.

Salary in the Lecturer scale, up to £3,045 p.a. Superannuation benefits under FSSU.

Application forms and further details available from the Assistant Secretary (Personnel) (N), The Royal Veterinary College, Royal College Street, London NW1 0TU. (1623)

UNIVERSITY OF WESTERN AUSTRALIA PERTH

Applications are invited for the following appointments from as early as possible in 1974:

ANATOMY

SENIOR LECTURER or LECTURER in Anatomy or Human Biology in the Department of Anatomy. This post could be of interest to a medically qualified person who has experience in the field of gross anatomy teaching and its clinical applications. Alternatively, an individual with training in physical anthropology who can teach gross anatomy to medical and science students would also be suitable. Research support for a major project in the physical anthropology of the Western Australian Aboriginal population is very likely to be available from the Australian Institute of Aboriginal Studies. Further information can be obtained from the Head of the Department, Professor D. B. Allbrook.

MEDICINE

ASSOCIATE PROFESSOR (1 position), SENIOR LECTURER (2 positions), LECTURER (2 positions) and LECTURER (temporary appointment for 1974) in the Department of Medicine. The Department includes teaching beds at each of the following hospitals: Fremantle Hospital, Repatriation General Hospital Hollywood, Royal Perth Hospital and Sir Charles Gairdner Hospital. The present research interests of the Department are gastroenterology, cardiology and renal disease. The appointees will be responsible for inpatient and outpatient care, teaching and research. They may be located at one or other of the University teaching hospitals. Candidates must have a medical qualification, registrable in the State of Western Australia, and the MRACP or an equivalent higher qualification is essential.

The salary ranges are: Associate Professor—\$A15,940 p.a.; Senior Lecturer—\$A12,268-14,308 p.a.; Lecturer—\$A8,698-11,982 p.a. The appointees in Medicine will also be entitled to the following differentials for clinical responsibilities: Associate Professor—\$A3,000 p.a.; Senior Lecturer and Lecturer—\$A2,500 p.a. Permanent conditions of appointment will include superannuation similar to FSSU, fares to Perth for appointee and dependent family, removal allowance, study leave and long service leave and housing loan scheme. A temporary appointee from within Australia will be entitled to fares to Perth for himself and wife, and from elsewhere to appointment expenses up to \$A1,000. Further information is available from the Staffing Officer.

Applications in duplicate, stating full personal particulars, qualifications, experience and earliest date of availability, should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia 6009, by December 15, 1973. Candidates should request three referees to write immediately to the Staffing Officer. (1625)

VICTORIA UNIVERSITY OF WELLINGTON NEW ZEALAND

LECTURESHIP IN MATHEMATICS

Applications are invited for the above-mentioned post in the Department of Mathematics. Applicants should have qualifications in mathematical statistics together with some practical experience in the application of statistics. Within the Department and Applied Mathematics Division research is undertaken in Markov processes, point processes, applications of statistics in geophysics, time series, optimization theory.

Salary range: NZ\$6,575-NZ\$8,343 p.a. Superannuation is available on an FSSU basis and an allowance is made towards travel and removal expenses.

Further particulars of the post, together with conditions of appointment and application procedure available from the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF.

Applications close on February 28, 1974. (1629)

Organic Chemists

Roche Products Limited is part of one of the world's leading Pharmaceutical Companies, offering research facilities of the highest standard at new laboratories in Welwyn Garden City, Hertfordshire. A variety of project groups, bringing together various scientific disciplines ensure that there are opportunities at all levels for synthetic organic chemists and technicians wishing to develop their talents and contribute towards the solution of challenging problems. We have openings for:

Scientists

Ph.D. Chemists to undertake creative research and direct the work of small chemical groups in the field of research for medicinal products.

Assistants

H.N.C., G.R.I.C. or first degree Chemists to carry out practical research in various fields.

Technicians

An opportunity for those with at least 'O' level and preferably 'A' level or O.N.C. Chemistry to develop practical skills, working as part of a team with a chance to undertake further study through day release.

All positions carry excellent Conditions of Service and fringe benefits. Further details of the openings available, together with an application form and Company booklet may be obtained from the Senior Welwyn Personnel Officer.



ROCHE

Roche Products Limited
Welwyn Garden City Hertfordshire AL7 3AY

(1553)

National Development Programme in Computer Assisted Learning Programmer-Scientist

Applications are invited for three posts of Development Officers (Computing) at University College London, Chelsea College London and University of Surrey, Guildford, in connection with a joint project on the use of Computers in the Undergraduate Science Curriculum, which is part of the National Development Programme in Computer Assisted Learning. The work involves close co-operation with academic staff in the preparation of computing programs, to be incorporated in teaching packages and in their documentation. Candidates should have graduate level qualifications and substantial programming experience, a background of science would be an advantage. The posts are temporary, in the first instance for two years, within a basic salary range £1,929 to £2,553 depending on age, qualifications and experience.

Further particulars can be obtained from the Project Director, Professor L. Castillejo, Department of Physics and Astronomy, University College London, Gower Street, London WC1E 6BT. (1560)

NATIONAL INSTITUTE OF AGRICULTURAL BOTANY TECHNICAL OFFICER

required in Cereals Section, Systematic Botany Branch. A degree in Botany or Agriculture with appropriate postgraduate experience and a knowledge of cereal varieties required. Salary scale £1,402-£1,925 or £2,087-£3,640, depending on age, qualifications and experience. Further particulars and application form from the Establishments Officer, NIAB, Huntingdon Road, Cambridge, CB3 0LE. (1612)

May & Baker Ltd

Physiologists/Pharmacologists

Applications are invited from graduate pharmacologists or physiologists interested in a career in the development of new therapeutic agents for the following posts:

Post-Doctoral Research Scientist for work with a team engaged in the study and development of new anti-asthmatic agents including prostaglandin-like drugs. Recent developments are most interesting and the work should have great appeal for a good research-orientated scientist interested in seeing a practical outcome to his work.

Post-Doctoral Research Scientist for work on gastric secretion. To develop and extend work of considerable promise already in progress leading to a new agent for the treatment of gastric and duodenal ulcers.

A Research Assistant with a good first degree together with some experience in drug research for work with a team involved in the study of new drugs for the treatment of coronary heart disease and atherosclerosis. Work of considerable interest is already in progress.

The research facilities provided by the May & Baker Research Institute are recognised as excellent. Team work is encouraged, as is publication in scientific journals and attendance at meetings of scientific societies.

May & Baker provide first-class conditions of employment including a highly competitive starting salary and contributory pension scheme with free life assurance cover.

Assistance towards removal expenses may be considered in suitable cases. Please apply in writing with details of qualifications and experience to The Personnel Manager, May & Baker Ltd., Dagenham, Essex RM10 7XS, quoting reference number 292/N/73.



M&B May & Baker

(1572)

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SCIENCE PUBLISHERS

have a vacancy for a

SENIOR EDITORIAL ASSISTANT

to work on the preparation and publication of research journals and monographs. Fields of interest vary over natural and environmental science. Applicants should have a science degree, with mathematics to at least A level, and be interested in publishing. Previous experience is not essential, but will be considered in assessing salary.

Write, giving full details, to Dr J. H. Ashby, Pion Ltd., 207 Brondesbury Park, London NW2 5JN. (1563)

LISTER INSTITUTE OF
PREVENTIVE MEDICINE

A TECHNICIAN with HNC or equivalent qualifications in Biochemistry, and a Junior Technician with 'A' levels in Chemistry and Biology, are required in the Biochemistry Department to assist in investigations on the immunochemistry and biosynthesis of blood group specific glycoproteins.

Applications in writing to Professor W. M. Watkins, Lister Institute, Chelsea Bridge Road, London SW1W 8RH. (1599)

BASIC GRADE BIOCHEMIST

DEPARTMENT OF CLINICAL CHEMISTRY

Applications are invited for the above post. Applicants should have an Honours degree in Biochemistry, Chemistry or one of the biological sciences, or hold Associate or Graduate Membership of the Royal Institute of Chemistry. Whitley Council salary and conditions of service.

Application forms from Personnel Department, Guy's Hospital, London SE1; 01-407 3662, ext. 68. (1552)

WHITTINGTON HOSPITAL

HIGHGATE HILL, LONDON N19 5NF

BASIC GRADE BIOCHEMIST required in the Endocrine Laboratory. Previous experience in Endocrine work is not essential as training will be given.

Apply to the Hospital Personnel Officer giving details of qualifications and experience and the names and addresses of two referees. (1549)

TECHNICIAN and JUNIOR TECHNICIAN required for Chemical Pathology Department to work on development of methods for assay of steroid hormones, lipids etc. Candidates qualified in chemistry, biochemistry or medical laboratory sciences preferred. Salary within scale £1,440-£2,292 plus £126 p.a. L.W. for Technician of £762-£1,396 p.a. plus £126 p.a. L.W. for Junior Technician. Apply The Secretary, St. Mary's Hospital Medical School, Paddington W2 1PG, quoting Ref. TCP 2. (1545)

UNIVERSITY OF LEEDS. Laboratory Technician Grade 6 required in the Department of Physiology. Responsibilities would include the operation of teaching laboratories for medical and science students and the supervision and training of subordinate staff. Assistance with the administration and forward requirements of the department would be expected. Apply by letter, stating age, qualifications and experience, to Mr E. French, Department of Physiology, Medical Multipurpose Building, Mount Preston Street, Leeds 2. (1575)

TWO JUNIOR TECHNICIANS required to assist in research into the role of hormones in the onset of labour. This is an MRC project for three years. Salary on the Whitley scale, depending on age and qualifications. Apply, giving full personal details, to Laboratory Administrator, Nuffield Department of Obstetrics and Gynaecology, John Radcliffe Hospital, Headington, Oxford. (1564)

PRINCIPAL LECTURER/SENIOR LECTURER in Pharmacology required by Liverpool Polytechnic, School of Pharmacy. Applications are invited from graduates in Pharmacy, Pharmacology, or related fields with specialisation in Pharmacology, who have a higher degree together with appropriate academic and research experience. The person appointed to the Principal Lecturer post will have overall responsibility for the development of undergraduate work in Pharmacology and will be expected to promote postgraduate studies and research work. An appointee to the Senior Lecturer post will contribute to undergraduate and postgraduate teaching and will be expected to engage in research. Excellent facilities are available and a new animal house is nearing completion. Salary: Principal Lecturer—£3,581 to £4,499 per annum; Senior Lecturer—£3,291 to £3,928 per annum. Details available from: Staff Office, Department N, Liverpool Polytechnic, Richmond House, 1 Rumford Place, Liverpool L3 9RH.

The National Radiological Protection Board

HARWELL

require a

SCIENTIST

for the

BIOLOGY DEPARTMENT

of the

RESEARCH AND DEVELOPMENT DIVISION

to join the Biophysics Group whose research programme includes a study of the deposition of radioactive aerosols in lung. The work involves both an experimental investigation and the development of a mathematical model for the calculation of aerosol deposition in lung.

The post is at the Board's Headquarters at Harwell. Applicants should have a first or good second class honours degree in a physical or biological science. Appointment will be in the grade of Scientific Officer or Higher Scientific Officer depending upon qualifications and experience. The salary scales appropriate to these grades are:

Scientific Officer	£1,415-£2,330 per annum
Higher Scientific Officer	£2,225-£2,855 per annum

For further information and an application form write or phone:

The Personnel Officer (A42/N7),
National Radiological Protection Board,
Harwell, Didcot, Berks.

Telephone: Rowstock 600 (STD Code 023-583) Extension 33.

(1607)

UNIVERSITY OF ESSEX

Department of Biology

Biology is an important new area of expansion at Essex University. Dr. J. M. Ashworth has been appointed to the first Chair in the Department, and Biological Sciences will be offered as an Honours Degree scheme to undergraduates entering in October 1974. Applications are now invited for the following appointments:

Senior Lecturer/Lecturer

(£4,368-£5,496 or £1,929-£4,548) with particular interests in

Genetics

for appointment from April 1974. Reference PS/49/N.

Two posts of Lecturer

(£1,929-£4,548) in the field of

Cell Biology

for appointment from October 1974. Reference PS/50/N.

Applications (four copies, quoting appropriate reference), should reach the Registrar, University of Essex, Wivenhoe Park, Colchester CO4 3SQ, from whom further particulars are available, by 10th December, 1973.

(1591)

CHEMIST

With Feed Formulation Experience

Zambia K8000+car

We are looking for a Chemist whose experience is supported by a knowledge of nutritional matters in the cereals-based human foods area and a desire to make a management contribution to the company's future. He will join our associate, the National Milling Company, which is engaged in flour and maize milling and the production of a range of stockfeeds. Based in Lusaka and reporting to the Managing Director, he will be responsible for stockfeed formulations; advising on specifications and purposes of a range of domestic foods based on cereals; and for co-ordinating laboratory work and advising on scientific techniques and procedures. He will be a member of the management committee and be expected to contribute to the overall development of the company's business. Considerable customer contact and some travel are involved.

This key position calls for candidates aged 30+ with feed formulation experience, a sound analytical background and a knowledge of human nutritional problems. Experience in commercial management, especially overseas, would be an advantage.

Starting salary, K8000 (about £4,800); a gratuity of 20% of total salary earned during the contract period will be paid on satisfactory completion of the contract. Three-year contract with renewal option. Other benefits include: return economy air passages for the employee and his family; rent-free furnished accommodation or housing subsidy; education allowance and one return air passage annually for each child above primary stage being educated outside Zambia; six weeks' annual leave.

Please write in confidence, quoting reference U.768, to:

D. Drayton, Management Resources Manager, Spillers Limited, Old Change House, 4-6 Cannon Street, London EC4M 6XB.

 **Spillers**

(1596)

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG, SOUTH AFRICA LECTURER IN MICROBIOLOGY

Applications are invited for the above post in the Department of Botany. A special knowledge in microbial metabolism and/or microbial industrial applications would be an advantage but not essential for the position offered. The two-year degree course, which is in the process of development caters for both pure and applied aspects of microbiology.

Salary will be in the range of R5,520-R7,935 (£3,350-£4,800 approximately), depending on the appointee's qualifications and experience. Benefits include an annual bonus, pension and medical aid facilities, and a housing subsidy (if eligible).

Intending applicants should obtain the information sheet relating to this post from the Registrar, University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, South Africa, with whom applications should be lodged not later than December 15, 1973. The information sheet may also be obtained from the London Representative, University of the Witwatersrand, Chichester House, 278 High Holborn, London WC1, with whom a copy of the application should be lodged. (1567)

UNIVERSITY OF HULL DEPARTMENT OF PLANT BIOLOGY

A vacancy exists for a RESEARCH TECHNICIAN (Grade 4) to work in the Biochemistry Section of the Department; to undertake culture of micro-organisms and extraction of materials using standard biochemical techniques. There will be some responsibility for preparations of teaching materials and for disciplinary aspects of the Section. Applicants should have 7/9 years relevant experience, together with an HNC or equivalent qualification. Salary on scale £1,848-£2,163.

Applications, quoting the names of two scientific referees, to the Technical Staff Officer, University of Hull, by November 26. (1621)

UNIVERSITY OF NEW SOUTH WALES SCHOOL OF BOTANY LECTURERS

Salary \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

Two vacancies. High academic qualifications in botany or agricultural science required. Appointees will teach in ecology, algology, cryptogamic botany or cytotoxicology and may contribute to an integrated first year biology teaching programme.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on December 7, 1973. (1538)

SOUTHAMPTON UNIVERSITY HOSPITALS PRINCIPAL SCIENTIFIC OFFICER (IMMUNOLOGY)

As part of a Regional Immunology Service being established by the Wessex Regional Hospital Board, a Principal Scientific Officer is required to help establish and run a service for assessing immunological competence in man. Previous experience in molecular and/or cellular immunology is required. There will be some time available for research, and there is opportunity for liaison with research teams.

Salary £3,516-£5,499 (rise pending) with N.H.S. superannuation.

Enquiries to Dr. G. T. Stevenson, Director, Tenovus Research Laboratory (Telephone Southampton 777222 Ext. 3451). Job descriptions from and applications to the Personnel Officer, Southampton University H.M.C., 119 Tremona Road, Southampton SO1 6HU.

Closing date December 1, 1973.

(1638)

AGRICULTURAL RESEARCH COUNCIL

UNIT OF MUSCLE MECHANISMS AND INSECT PHYSIOLOGY, OXFORD

Applications are invited for the posts of BIOCHEMICAL RESEARCH ASSISTANT and TECHNICIAN to assist in the preparation and analysis of contractile proteins. A degree in biochemistry or experience of protein preparation is desirable. The appointment will be on University scales.

Technician Grade 3, £1,539-£1,734 (under review). Graduate Research Assistant £1,491-£2,556.

Applications, accompanied by curriculum vitae and the names and addresses of two referees should be sent to Professor J. W. S. Pringle, Department of Zoology, South Parks Road, Oxford, OX1 3PS, by November 30, 1973.

(1639)

UNIVERSITY OF NEW SOUTH WALES SCHOOL OF CHEMISTRY LECTURER

A Lecturer in Chemistry is required for academic duties primarily concerned with first year chemistry. Opportunity exists to give other specialised lectures and carry out research. High academic qualifications and some tertiary teaching experience in chemistry required.

Salary: \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on December 14, 1973. (1537)

UNIVERSITY OF NEW SOUTH WALES SCHOOL OF MICROBIOLOGY LECTURER

Salary: \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

PhD or equivalent qualification, together with training and research experience in general field of microbiology, required. Experience in areas of food or industrial microbiology would be relevant.

Details of appointment including superannuation, study leave and housing scheme, may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on December 14, 1973. (1536)

LECTURES AND COURSES

UNIVERSITY OF MANCHESTER DIPLOMA IN BACTERIOLOGY

Applications are invited for admission to the Diploma in Bacteriology course to be held in the session 1974/75. The course is designed to give training and experience in aspects of bacteriology and animal virology which are of general importance in the application of the subject to different specialised fields. Applicants must have qualified in medicine, veterinary medicine, or other branches of science, and have had substantial postgraduate practical experience in bacteriology. Medical Research Council awards may be available to suitably qualified British subjects resident in the United Kingdom.

Forms of application may be obtained from the Department of Bacteriology and Virology, University of Manchester, Stopford Building, Oxford Road, Manchester, M13 9PT, and should be returned as soon as possible, and in any case not later than February 1, 1974. (1550)

TOXICOLOGY RESEARCH

The Toxicology area of our Research Department, situated in modern, well-equipped laboratories in Nottingham, continues to expand as more projects reach advanced stages of investigation and new projects are initiated. Two new opportunities have been created for biological scientists to join the team engaged in the safety evaluation of new medical, animal health and crop protection products.

Reproduction Toxicologist

Will assume responsibility for all reproduction and teratological investigations and additionally, will contribute towards technical documents for product registration in the U.K. and overseas. Applications are invited from good honours graduates in a biological science possessing relevant post graduate experience. (Ref: D 101)

Non-Medical Clinical Biochemist

Will assume responsibility for the development of new assay procedures and for research in biochemical pharmacology relevant to the toxicological assessment of new drugs. Applicants should be keen to innovate and, desirably, have experience of clinical biochemistry in hospital or industrial laboratories. (Ref: D 102)

Conditions of employment are attractive, and include good profit sharing and contributory pension schemes. Some help with relocation expenses will be granted where appropriate.

Please write, giving brief details of age, qualifications and experience and quoting the appropriate reference, to:



J. F. Pattison, Employment Manager,
The Boots Company Ltd.,
Nottingham NG2 3AA

(1631)

NATIONAL RESEARCH COUNCIL, CANADA

Postdoctorate Fellowships in Government Laboratories 1974-75

The National Research Council of Canada offers Fellowships for 1974-75 tenable in its laboratories and administers additional Fellowships on behalf of the following Canadian Government Departments and Agencies: Agriculture Canada; Department of Communications—Communications Research Center; Department of Energy, Mines and Resources; Department of the Environment—Atmospheric Environment Service, Environmental Management Service, Canadian Forestry Service, Inland Waters Directorate, Fisheries and Marine Service, Fisheries Research Board of Canada, Marine Sciences Directorate; Health and Welfare Canada—Health Protection Branch; National Museums of Canada—Museum of Natural Sciences; Atomic Energy of Canada Limited.

An applicant should possess a Ph.D. degree from a recognised university, or expect to obtain such a degree before taking up an award. Candidates having equivalent research experience may be considered. Normally an applicant should not have reached his 36th birthday by March 31 of the year in which the Fellowship is to be taken up. Applicants exceeding this age limit should not be more than one year past Ph.D. graduation. There are no restrictions regarding nationality of applicants, but successful candidates must meet all Canadian immigration requirements. The competition closes on January 15, 1974.

Fellowships have an annual value of \$9,000 and are subject to Canadian income tax. A grant is provided towards the cost of travel.

Inquiries should be addressed to the Postdoctorate Fellowships Office, National Research Council of Canada, Ottawa, Canada K1A 0R6.

(1577)

UNIVERSITY COLLEGE CARDIFF

Applications are invited for the following vacancies:

RESEARCH FELLOW/SENIOR RESEARCH FELLOW IN ASTRONOMY

APPLIED MATHEMATICS DEPARTMENT

Salary Range: £1,929-£3,543/£3,708-£4,548. Duties to commence January 1, 1974. Closing date for applications November 15, 1973.

Applications, together with the names and addresses of two referees, should be forwarded to The Registrar, University College, P.O. Box 78, Cardiff CF1 1XL, from whom further particulars will be available. Please quote 0940.

(1543)

FELLOWSHIPS AND STUDENTSHIPS

THREE POST-DOCTORAL FELLOWSHIPS IN THE EARTH AND PLANETARY SCIENCES

The Lamont-Doherty Geological Observatory of Columbia University invites scientists interested in any field of the earth and planetary sciences to apply for the following Fellowships.

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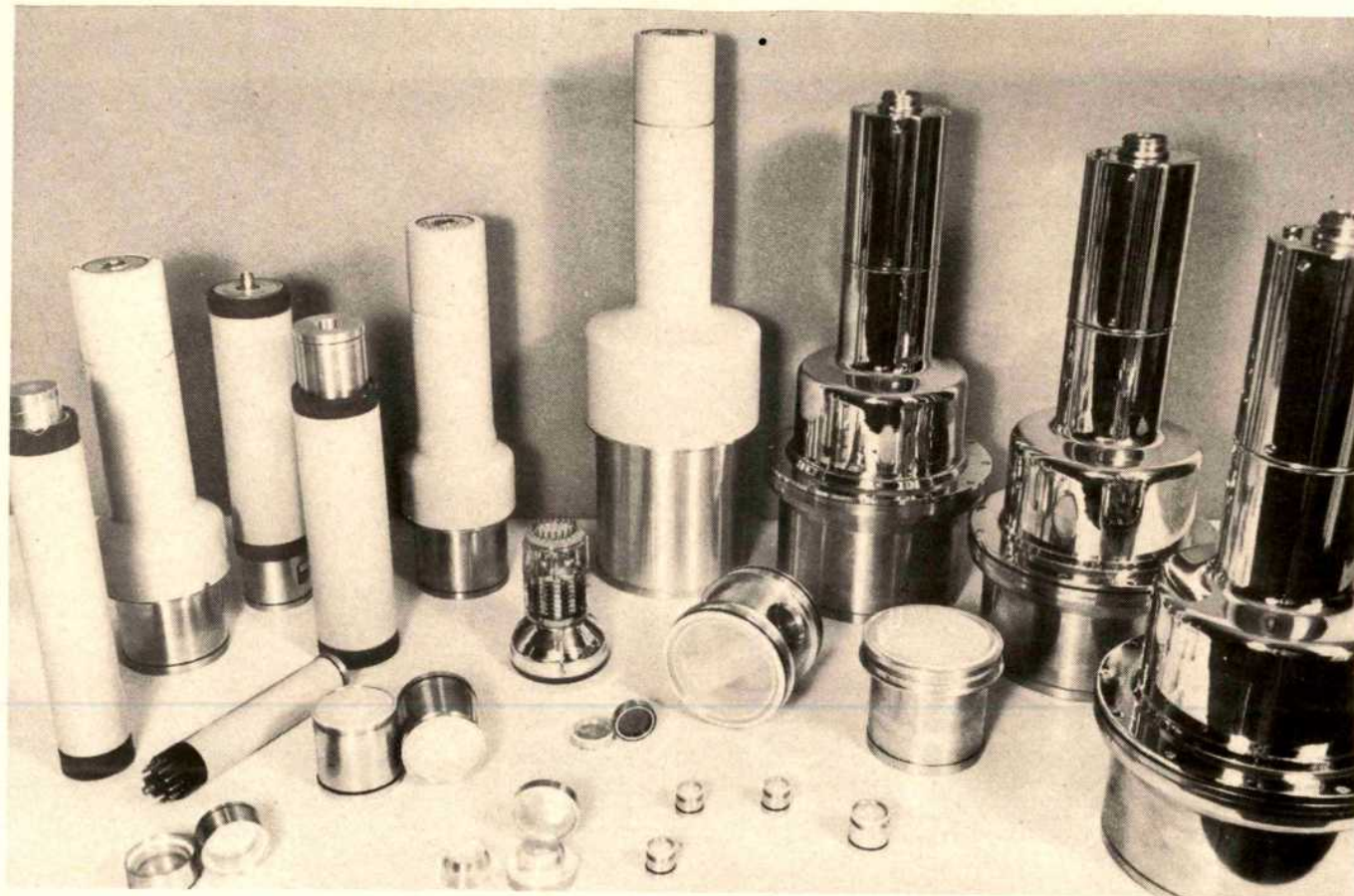
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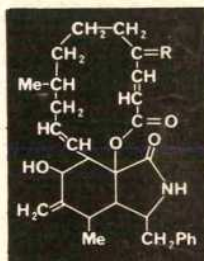
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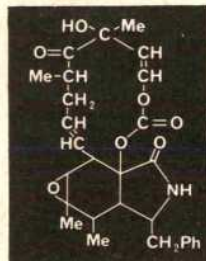
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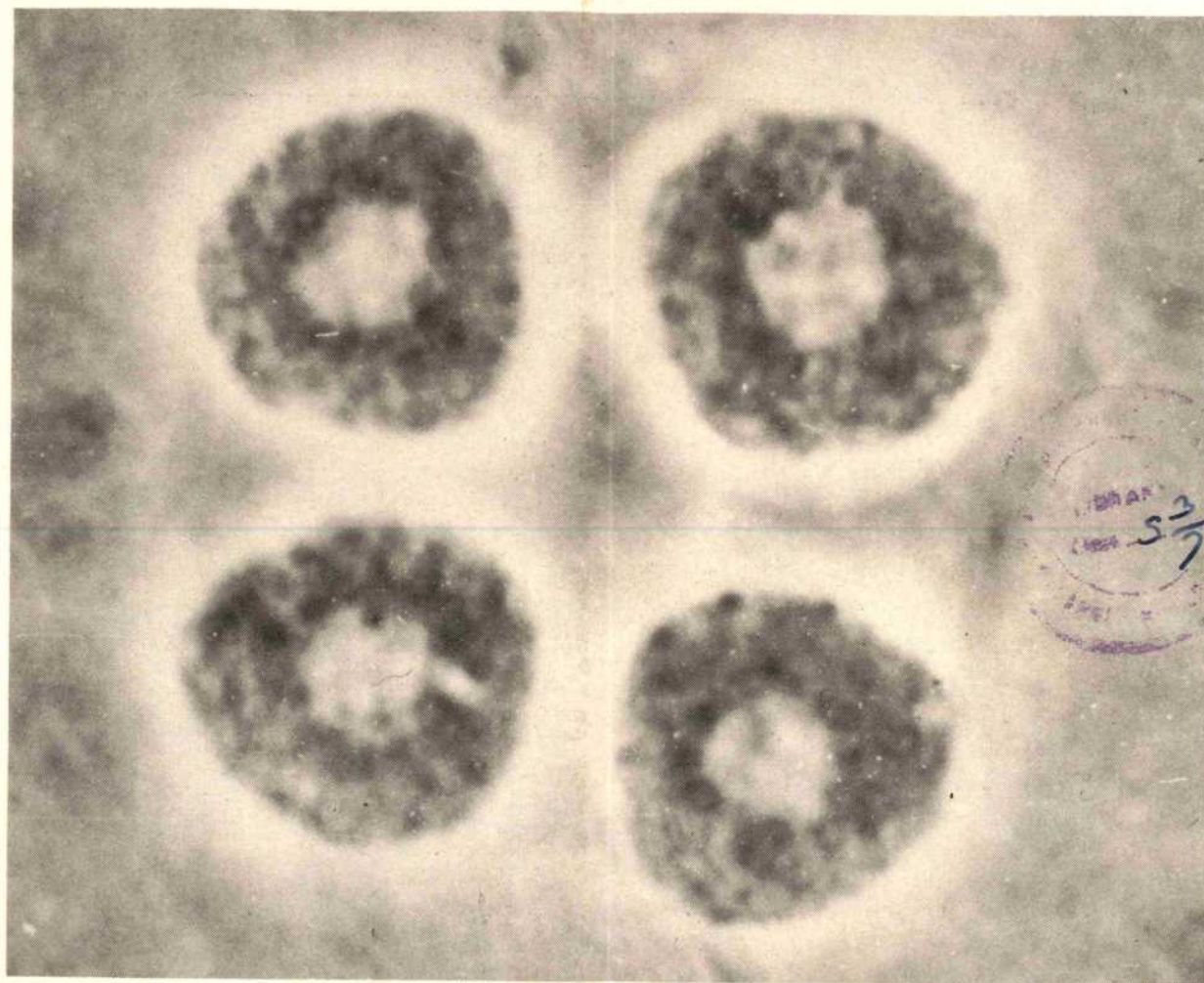
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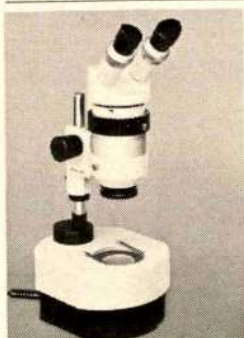
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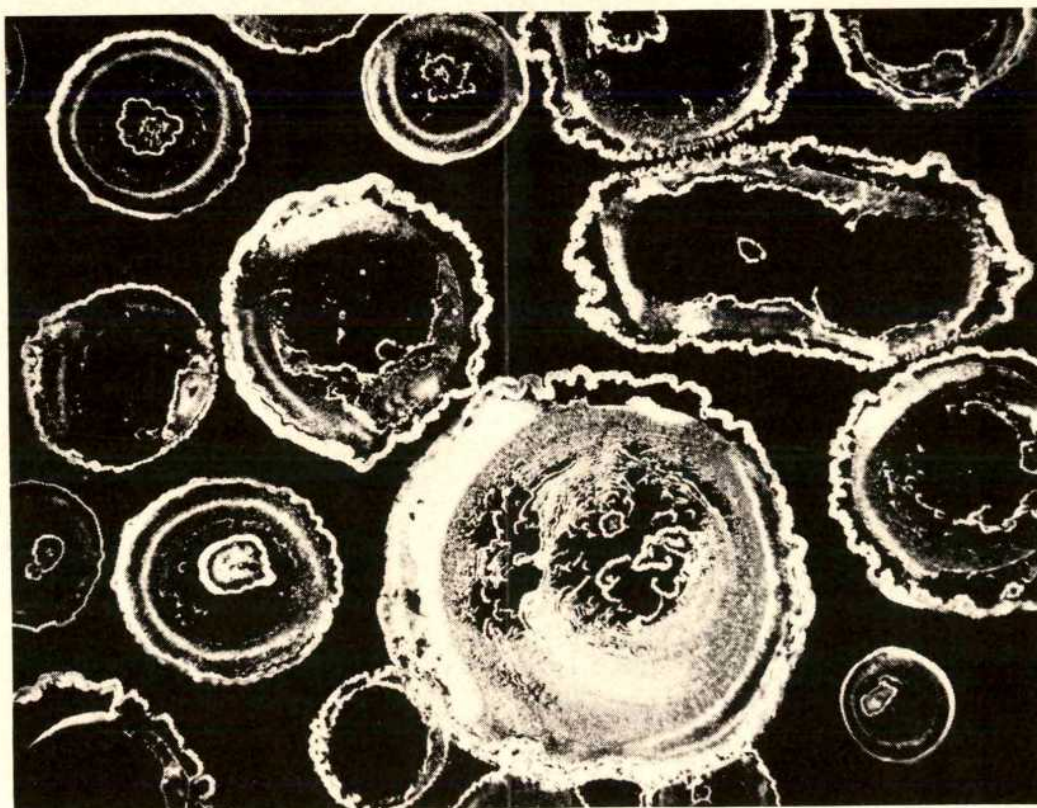
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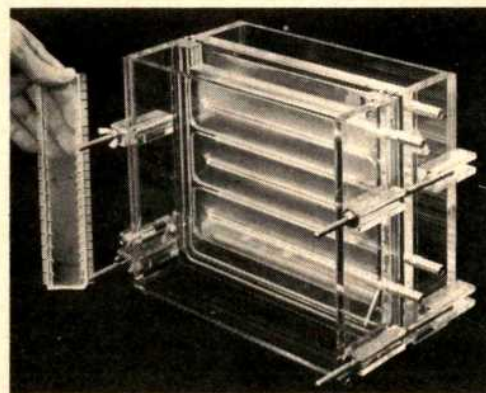
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	Page		Page
A Broader Debate on Energy	179	Magnetism —Force on a wire in a magnetic field depends only on total current—LOWES (Newcastle upon Tyne)	208
NEWS		Plate tectonics —Evidence for the opening of the South Atlantic in the Early Cretaceous—LARSON and LADD (Columbia)	209
More Uranium Found in Britain/Steel/Nuclear Reactors/Automobile Pollution/Royal Society/Short Notes	180	Atmosphere —World-wide source of leaf-derived freezing nuclei—SCHNELL and VALI (Wyoming)	212
NEWS AND VIEWS			
Redshifts of Quasistellar Objects/From Cyclic AMP to Cyclic GMP/Immunopathology of Parasitic Infection/Contraception/Protein Synthesis/Insect Physiology/Silica/Palaeontology/Selenology	185	Biological Sciences	
ARTICLES		Transformed cells —Rapid screening assay for revertants derived from cells transformed by MSV—NOMURA, DUNN and FISCHINGER (National Cancer Institute, Bethesda)	213
Submillimetre Astronomy —SIMON (State University of New York, Stony Brook)	193	Prostaglandins —Role as potentiators of increased vascular permeability in inflammation—WILLIAMS and MORLEY (Kennedy Institute of Rheumatology, London)	215
Cell growth —Conditions limiting multiplication of fibroblastic and epithelial cells in dense cultures—DULBECCO and ELKINGTON (Imperial Cancer Research Fund)	197	—Potentiation of oedema-producing capacity of other inflammatory mediators—MONCADA, FERREIRA and VANE (Royal College of Surgeons)	217
—Role of the diffusion boundary layer in contact inhibition of growth—STOKER (Imperial Cancer Research Fund)	200	Rhodopsin —Incorporation of rhodopsin proteolipid into bilayer membranes—MONTAL and KORENBROT (Mexico)	219
LETTERS TO NATURE		Phage λ —Fate in non-immune germ-free mice—GEIER, TRIGG and MERRIL (NIMH, Bethesda)	211
Physical Sciences		Protoplasts —Nuclear divisions occurring in isolated protoplasts from pollen tetrads of <i>Datura metel</i> —RAJASEKHAR (Bhabha Atomic Research Centre, Bombay)	223
QSOs —A double object—WAMPLER, BALDWIN, BURKE, ROBINSON (California, Santa Cruz) and HAZARD (Cambridge)	203		
—Discrepant redshifts of QSOs in clusters of galaxies and a close QSO pair—HAZARD (Cambridge), JAUNCEY (Cornell), SARGENT (Hale Observatories), BALDWIN and WAMPLER (Lick Observatory)	205		

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 188 to 191.

(Continued overleaf)

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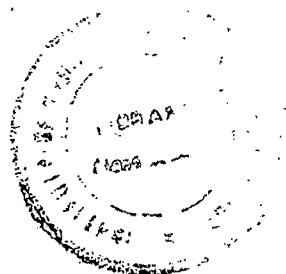
	Page		Page
Schistosomes —Secretion of migration inhibitory factor by intact schistosome egg granulomas <i>in vitro</i> —BOROS, WARREN and PELLEY (Case Western Reserve)	224	Developmental Biology: Its Cellular and Molecular Foundations , Maurice Sussman (J. M. ASHWORTH)	232
		Avian Biology , Donald S. Farner and James R. King (editors) (KNUT SCHMIDT-NIELSEN)	233
General		Particle Physics: An Introduction , M. Leon (DAVID J. MILLER)	233
Demography —Ignorance about limits to growth—BURKE (Waterloo, Ontario)	226	Functional Anatomy of the Newborn , Edmund S. Crelin (VICTOR DUBOWITZ)	233
BOOK REVIEWS		Introduction to Food Science and Technology , George F. Stewart and Maynard A. Amerine (JOHN WOODMAN)	234
Autocritique de la Science, Alain Jaubert and Jean-Marc Levy-Leblond (editors) (JOHN ZIMAN)	231	Ethylene in Plant Biology , Frederick B. Abeles (L. J. AUDUS)	234
The Effects of Irradiation on the Skeleton, Janet M. Vaughan (F. W. SPIERS)	231	CORRESPONDENCE	
Organisation in Animal Communities: Experimental and Naturalistic Studies of the Social Behaviour of Animals, Hilary O. Box (MARIAN DAWKINS)	232	Smoking in Pregnancy (William H. James)	235
Seed to Civilization: The Story of Man's Food, C. B. Heiser, jun. (MAGNUS PYKE)	232	Obituary—Professor E. A. Stewardson	235
		Announcements—Appointments/International Meetings	236

Next Monday's issue will include

- Cosmic rays**—Consistency of source abundances with explosive nucleosynthesis—KOSLOVSKY and RAMATY (NASA, Goddard Space Flight Center)
- Radio astronomy**—Detection of Cyg A galaxy—PECKHAM (Manchester)
- Geophysics**—Rock of Grenville age from Rockall Bank—MILLER and MATTHEWS (Cambridge) and ROBERTS (Institute of Oceanographic Sciences)
- Catalysis**—Oscillations during catalytic oxidation of carbon monoxide on platinum—DAUCHOT and Van CAKENBERGHE (Mons)

Next Wednesday's issue will include

- Globin synthesis**—Translational control by haemin in *Xenopus* oocytes—GIGLIONI, GIANNI, COMI, OTTOLENGHI (Milan) and RUNGGER (Geneva)
- Cyclic AMP**—Leakage of cyclic AMP from human diploid fibroblasts in tissue culture—FRANKLIN and FOSTER (ICI Pharmaceuticals, Macclesfield)
- Methylmercury**—Effect of phenobarbitone on biliary excretion in rats and mice—MAGOS (MRC, Carshalton) and CLARKSON (Rochester)
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A Broader Debate on Energy

WITH the sudden attention that energy and its wise use is receiving world-wide, it was appropriate that the Royal Society should have convened a meeting to discuss 'Energy in the 1980s' last week. By an amusing coincidence, it started on the day the advertising signs were extinguished in Piccadilly Circus. There was more to our interest in the meeting, however, than simply the (fulfilled) expectation of adding to our knowledge in the field. If scientists and technologists are to speak to the public beyond their own community in a manner that will stimulate discussion and understanding, form is every bit as important as content, so we were particularly interested in the shape that the meeting would take. Two weeks ago *Nature* reported unfavourably on an energy meeting convened by the Royal Society of Canada (246, 56; 1973) largely on the grounds of its conventional format; could this one produce something new?

That it did not was no discredit to Sir Peter Kent who had assembled a distinguished list of speakers. Relevance, however, increases greatly with the proximity of the threat, and since the meeting had been announced, the question had changed dramatically from being what will we have in the 1980s to what will we make do with in 1974. One by one specialists discussed dispassionately their particular interests and supplied a multitude of data but the projections into the 1980s were cautious and assumed a relatively undisturbed society and no surprises, pleasant or otherwise. What was needed to complement these strands was a shuttle to weave cross threads and put the story together according to different patterns. What happens to the projections when oil supplies are cut by 10% in 1973? If the nuclear programme falters how are the other resources strained? If several as yet underdeveloped countries with large populations suddenly acquired an appetite for energy how would projections be affected? (We are, after all, at present seeing the consequences in the world food situation of the growing appetites of developing countries for protein.) And perhaps the key question—is energy saving, either voluntary or compulsory, going to make any impact on energy needs? It may be that what meetings of this sort need is the stimulus of a longish paper which has been read by everyone previously and which is sufficiently provocative that experts can spend their time dismembering and rebuilding rather than pursuing independent paths. Certainly some sort of interlocutor would be a useful addition.

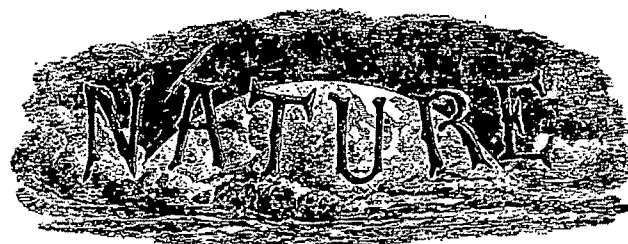
As it happened, the lack of a feel for total situations at the meeting was balanced by the simultaneous launching (surely no accident) of a document by the Friends of the Earth. This booklet, 'World Energy Strategies' by Amory Lovins, is worth reading if only because the author does attempt a synthesis. He works from the hypothesis that a "resource inventory would by itself be useless . . . energy constraints are not mainly dictated by physical scarcity, but are geopolitical, environmental and socio-technical".

Mr Lovins sees coal as the short and medium term solution to the energy problem. On the way to this con-

on the need for constraint in energy usage, particularly in the United States, some caustic words on the safety risks of nuclear fission and some hopeful thoughts on coal. He concludes that "the problems of coal are substantial but can be solved" whereas "governments should suspend their nuclear programmes until enough infallible people can be found to operate them for the next few hundred thousand years". This is an outspoken and biased point of view. Mr Lovins is prepared to give coal the benefit of every doubt, nuclear energy the benefit of none. Nuclear energy has to be judged not only by technical standards but by ethical considerations, whereas coal, the pursuit of which mars thousands annually but which lacks the magical ability to afflict unborn generations, is let off the social hook with a naïve reference to a recently opened Illinois deep mine which "is said to use every kind of safety and health precaution yet still is profitable." We are not the first to point Mr Lovins to Otto Frisch's delightful essay 'On the feasibility of coal-driven power stations'.

Nonetheless, Mr Lovins is a great asset and should not be lightly dismissed. For too long, discussion of broad multidisciplinary issues in the United Kingdom has been subordinated to the pursuit of excellence in individual fields. Decision making has been regarded as so much a province of government that national discussions of policy issues have been sadly lacking. For all that we may disagree with the Mr Lovinses, we need them in order to open up the debate. Preferably we need them on the same platforms as the experts and certainly we need them to make a nuisance of themselves.

100 Years Ago



A HEALTHY HOUSE

What a House should be, versus Death in the House. By William Bardwell, Architect and Sanitary Engineer. (London: Dean and Son.)

It would be interesting to have had some references given to sanction our author in claiming the authority of the Duke of Wellington, together with that of Aaron and the High Priests, his successors, for the practice of placing their beds nearly north and south so as to be in the line of the magnetic current. The theory no doubt has its advocates, but can hardly be of universal application, as there are many sound sleepers at all degrees of orientation.

NEWS

More Uranium Found in Britain

THE Institute of Geological Studies reported this week that uranium is to be found in North Wales, the Southern Pennines, the South Wales coalfield, the Midlands as well as in the north of Scotland and south west England. (*Uranium Mineralisation*. . . , S. H. U. Bowie, D. Ostle and C. B. Campbell, IMM Applied Earth Science Transactions Section B, November 1973.)

Deposits in Scotland and in south west England have been previously reported by the IGS. A few thousand tons of uranium in the oxide form, U_3O_8 are to be found in Caithness and Orkney and a few hundreds of tons in the south west of England.

The extent of the deposits now found in Wales and other parts of England are not revealed but the strength, in terms of parts per million of uranium ore, makes it clear that the deposits are at present not of economic significance. But they represent reserves, which if they turn out to be of sufficient tonnage, might well prove to be of strategic importance. The possibility of mining these deposits will not arise until the high quality ore at present being mined in Canada and South Africa are worked out and the cost of ore inexorably rises.

The deposits in the Orkneys are low grade and widespread but Dr Bowie and colleagues report that in places the content of uranium in phosphatic rock is as high as 1,000 parts per million, amounting to 0.1% enrichment, which compares favourably with the quality of uranium ore now being mined in other parts of the world. But the uranium content of the dark shales in the Orkneys rarely exceeds 200 parts per million. In the south west of England, however, the ore is found in high grade concentrations but of low tonnage. The new survey revealed, however, several new sources of uranium but they are also of modest tonnage or low grades. At Fingle Bridge, a rich zone has been found of 0.5% enrichment which is over 5 feet wide.

At Luton on the western side of Dartmoor a vein has been found which is one foot wide, and a sample analysis showed that the uranium content was of the order of 3%. This same vein contains also copper, lead, silver and arsenic.

Several other sources of uranium have been found in the south west of England but the full extent of some of the deposits can not be revealed unless drilling takes place.

The present survey was restricted to sampling of stream water, sediment, wells and boreholes. When the terrain was suitable the countryside was scanned for evidence of radioactivity by carrying scintillation counters in vehicles and in some place by scanning for radioactivity on foot.

Of the newly reported finds of uranium, the IGS team reports that although some uranium is to be found in North Wales, it is not of economic grade. "The rocks represent a major crystal enrichment but no evidence has yet been found of uranium concentrations sufficient to produce deposits of potential value."

The uranium concentrations in the southern Pennines are very low (10-30 parts per million) but in the South Wales coalfield, concentrations of 270 ppm have been found. It is unlikely, however, that the element is present here in sufficient quantities to be of economic significance, according to Dr Bowie and colleagues. The highest concentration

of uranium found in the Midlands amounted to 162 ppm and this is in a shallow peat deposit.

No marked radioactivity was found in extensive examinations across the Midlands, from the Welsh borderland in Montgomeryshire and Radnorshire to Lincolnshire and Nottinghamshire except for some activity near the known outcrop of Cambrian shale near Nuneaton.

Uranium has never been mined on a large scale in Britain although it was obtained as a by product of a pitch blend mine near St Austell earlier this century. Britain, however, is not likely ever to produce enough uranium to fulfill its needs. The nuclear reactors at present in operation in Britain need more than a thousand tons of uranium a year to keep them in production. When it does become economic to think of mining uranium in Britain then the reported reserves (a few thousand tons of U_3O_8) represent at the present rate of usage, a few years' supply.

STEEL

European Opportunities

An improved coordination of steel research within Europe was called for by Dr Robert S. Barnes, director of research and development at the British Steel Corporation, last week. Dr Barnes, delivering the annual Hatfield memorial lecture, said that "the need to exchange technical views, to criticise, construct and develop cooperatively concepts for joint European research activity is now more necessary than ever it was".

Dr Barnes was critical of the arrangements existing at present within Europe for collaborative research in steel. The task of processing and assessing the waves of uncoordinated and untranslated proposals which sweep through the EEC and its advisory committees several times a year is too great, according to Dr Barnes. "The commission's advisory committees—there must be about a hundred of these—only deal with narrow technical areas and are often more concerned with technical details rather than with the broad needs for the individual research projects or with the eventual application of their outcome."

There is therefore a need for efforts to be concentrated on a few clearly defined and large projects, which for one

thing would ease the communication and administrative problems of steel research in Europe, said Dr Barnes.

In order to achieve these objectives, the European Commission will have to be advised in a different way. At present the commission's advisory experts are appointed as individuals and it would be advantageous if these experts represented the collective view of the European steel industry. Dr Barnes called for the industry to set up just such an organisation which would "produce and regularly update a strategy for collaborative research". It is possible that l'Association Européenne pour la Promotion de la Recherche Technique en Siderurgie could fill this role.

Dr Barnes also highlighted in his lecture a possible way of making steel in the future by using the gas emitted from a High Temperature Nuclear Reactor as a reducing agent. The gas would first be used to convert the iron ore to a pre-reduced iron. This would then be fed to an electric arc powered by electricity obtained from the waste heat of the first process.

Such direct use of nuclear power could be the way in which most steel will be made in the twenty-first century. It could, however, be introduced even sooner if the costs of using other forms of energy, such as coal or electricity, escalate faster than anticipated.

NUCLEAR REACTORS

Britain's Power Dilemma

THE miners, Arabs and power workers between them made life so bad for Britain's power industries last week that a meeting of the Nuclear Power Advisory Board, which was to take another step along the troubled road to choosing Britain's next reactor type, had to be cancelled. Everyone had too much on their plates already.

An announcement is expected early next year from Mr Peter Walker, Secretary of State for Trade and Industry, on which type of reactor Britain is to build next.

The Nuclear Power Advisory Board has already had presentations from the chief parties interested in the choice and has learnt from the Central Electricity Generating Board that it wants to buy light water reactors from the United States—preferably Pressurized Water Reactors (PWRs) from Westinghouse.

The board argues that the light water reactors are cheaper and more proven than anything else available. The alternatives are fourfold. Britain could build more Advanced Gas Cooled Reactors. Five of these are being built. All of them are late, and the first is not due to produce full power until 1975.

Two of the other possibilities require development. These are the Steam Generating Heavy Water Reactor, a 100 MW prototype of which has been performing well at Winfrith in Dorset since 1967, and the High Temperature Reactor. But the board argues that it is too late to build SGHWR. It offers too little export or development potential, is more expensive than the PWR, a development programme would be required with all its attendant risks and substantial qualities of heavy water would be needed. The High Temperature Reactor also suffers from the need for a development programme. A 30 MW prototype has been operating since 1963, but 30 MW is a far cry from the 1,200 MW size that interests the CEBG. The board is relatively enthusiastic about the design, however, and would like to see a commercial plant built. But it does not want to use the HTR for the large scale programme it is envisaging—six to eight stations on order by 1980. It would rather see the design developed more slowly.

The final possibility is that another Magnox station could be built. In spite of corrosion problems, Magnox stations have performed well and last year produced some of the cheapest electricity. With some redesign work to remove corrosion problems more Magnox stations could be a reliable bet. But the board believes the cost to be prohibitive, perhaps £600 million a station as against about £400 million for a more modern design.

The argument is not quite as simple as the CEBG would have everyone believe. For a start it is unfortunate, to say the least, that the empty order books of the nuclear industry, the government's commitment to reach a decision soon and the CEBG's belief that it will need more nuclear stations by the end of the decade have all combined to force a decision now rather than in eighteen months or two years time, when it will be seen whether at least one of the Advanced Gas Cooled Reactors, costing between them rather more than £1,000 million, works. Equally the CEBG's calculations studiously ignore the question of foreign exchange. With a trade gap running at £289 million in a single month, the government cannot be eager to spend more money abroad than it has to. And a first PWR would be bought lock and stock, if not barrel, from the United States. As the CEBG sees it, Britain's GEC-dominated National Nuclear Corporation would provide the emergency core cooling system, the containment and the chemical engineering of the new station, but the remainder of the nuclear steam supply system would come from abroad.

And the question of safety remains to be answered. The United States Atomic Energy Commission has spent the past two years arguing in public and private about the effectiveness of the Emergency Core Cooling System (ECCS) that is a key part of the PWRs' defence system against a bad nuclear accident. Theoretically the ECCS douses the reactor core in water within seconds of, for example, a broken pipe or blocked pump cutting off the normal cooling water supply to the core. Without water, a dry core heats to 1,800° C within a minute, at which point the fuel and zirconium fuel cans being to melt. An hour after the loss of cooling water the core has flowed to the bottom of the reactor vessel accompanied by steam explosions which, combined with gas pressure, could split the reactor vessel, releasing fission products. A few hours after that, the molten core would have eaten through the reactor vessel and the concrete foundations.

The ECCS is designed to prevent this happening. But no practical test of the system has been made, and an AEC facility known as the Loss of Fluid Test Facility will not be ready to run the crucial experiments on what does actually happen to a dry core until 1975. Theoretical calculations suggested that the emergency core cooling system would prevent these events. But other sums produced different answers, and a small scale test on a simulated reactor core suggested that in the event of 30 to 100% of the cooling water leaving the reactor, only 10% of the emergency cooling water would reach the core. The Loss of Fluid Test should confirm

or quell these doubts. But the answers will not be available by January when Mr Walker has to make his decision.

The CEBG is of course aware of these problems. It has looked at the calculations at its nuclear laboratories at Cheltenham and concluded that the light water reactors are safe enough. But its conclusion is not going unchallenged. The Friends of the Earth have just launched a campaign on energy and its conservation. Their sister organisation in the United States has been at the forefront of the campaign against light water reactors. Last week a spokesman for the British end of the organisation said that "it is a little difficult to explain" how the CEBG has managed to satisfy itself about the safety of light water reactors while the Atomic Energy Commission is still sorting out the problem.

Aside from the safety matter, it is not at all certain that building PWRs will be as easy as the board maintains. Its interest lies in 2,400 MW stations consisting of two 1,200 MW sets. The largest PWR built and operating to date is 1,050 MW. And in spite of talk about buying proven designs, no reactor comes off the shelf. British industry will have to learn to build PWRs just as it has had to learn to build AGRs or would have to learn to build commercial HTRs or SGHWRs. Walt Patterson, a nuclear physicist who works with Friends of the Earth, says "the whole AGR fiasco is entirely conceivable as a re-run with light water reactors". Additionally the complaint is common within the industry and the United Kingdom Atomic Energy Authority that the CEBG cannot resist fiddling with power station designs.

A final question worth asking is why the government, the Atomic Energy Authority, the generating boards and the industry have the current problem to solve at all.

The CEBG seems happy to consign the AGR to oblivion. Yet it is the

Forthcoming Natures

NEXT week, *Nature* will contain a thirty-two page supplement reviewing science in Australasia.

Nature for Friday, December 14, will be a Christmas issue. In addition to the regular features there will be several pages of specially commissioned articles, chess problems and a quiz.

The two Friday issues of December 21 and 28 will be combined in one large edition that will be published December 21. *Nature Physical Science* and *Nature New Biology* will likewise be published in double issues on December 17 and December 19 respectively.

board that ordered the reactor in the first place, commissioned three separate designs and agreed to build these before a full prototype was constructed. (The Windscale AGR, well though it has run, is a far simpler machine than the commercial stations, built more for fuel testing than as a proper prototype.) The stations were all approved without detailed design work being undertaken.

It is a similar mess that everyone is trying to avoid this time. The choice is not an easy one. As Sir John Hill, Chairman of the Atomic Energy Authority, said at the Royal Society symposium on energy last week "all reactor systems have some problems". He also pointed out that "every time there is a major change of design there will be difficulties". It is possible that light water reactors will prove the final choice. But the CEBG should admit that the case is not as clear cut as it claims.

AUTOMOBILE POLLUTION

GM Breaks Ranks

by our Washington Correspondent
MOTOR manufacturers have recently failed in a last ditch attempt to keep exhaust catalysts off cars sold next year. For months, executives from the car industry have been badgering Congressmen and Senators, trying to win yet another delay in implementing the stringent exhaust emission controls specified by the Clean Air Act, and the matter finally came to a head early this month when the Senate Public Works Committee held a couple of days of hearings on automobile pollution. Spokesmen for the industry warmed over a number of old arguments, seized upon all kinds of real or imaginary fears, and invoked threats of economic and social disaster if the Clean Air Act is not soon modified. But the chief outcome seems to be a huge split in their own ranks.

They were arguing, essentially, for emission controls to be frozen at their present levels for the next two years, and for some rather more stringent controls to be imposed in 1977. Such a delay would put off the need to fit exhaust catalysts, since the present regulations can be met with engine modifications, and the clear intention is to use the breathing space to work to put off that fateful day entirely.

That, at least, is the position taken by representatives of Ford and Chrysler, who were unstinting in their criticisms of the catalyst. But witnesses from the other member of the big three, General Motors, broke ranks and came out with some extraordinary statements in support of the device. But they, too, want the controls relaxed, although only by a small amount.

strator of the Environmental Protection Agency, said that he is not prepared to recommend relaxing or delaying the standards, and the committee shows no sign of taking the initiative itself. Thus, as John J. Riccardo, president of Chrysler put it, since "action must be taken now, or it will be too late", exhaust catalysts will be fitted to cars sold next year.

It was a last ditch attempt by Ford and Chrysler because the Environmental Protection Agency has already given them the maximum amount of time available to meet the standards, and the only possible way to delay things further would be for Congress to modify the Clean Air Act. The act requires that 1975 model cars emit 90% less carbon monoxide and oxides of nitrogen than 1970 models, and that 1976 models emit 90% less oxides of nitrogen than 1971 models. Earlier this year, however, the motor manufacturers persuaded the Environmental Protection Agency to give them an extra year to meet the standards. But part of the EPA's bargain included a provision which requires that all 1975 model cars sold in California must meet strict emission controls—and that will need the use of exhaust catalysts on those cars. The rationale was to force catalysts to be introduced in California next year—1975 model cars will be unveiled in the Autumn of 1974—and nationwide a year later.

Ford and Chrysler executives argued, as they have done for the past two years, that the catalyst is inherently bad technology, and that they would like to use better devices, such as the stratified charge engine, if only they had the time to do it. But, if they are forced to clean up car emissions immediately, they have no alternative to sinking their money into exhaust catalysts at the expense of developing the other technologies.

Six months ago, that was also the complaint put out by General Motors, but at the hearings earlier this month, Edward N. Cole, the company's president, said bluntly that there is no need to modify the interim regulations set for California in 1975, and that the conventional engine equipped with catalytic converters will be the best method of cleaning up automobile pollution. Cole also said that GM cars will be able to meet the 1975 interim standards, and that catalysts will be fitted not only to cars sold in California, but to others as well.

The effect of the split in Detroit's previously united front had the effect of undermining many of the arguments put up for delaying the standards, and environmentalist witnesses at the hearings had little difficulty in playing off one statement from the car manu-

perhaps worth noting, in any case, that only a few months ago, when spokesmen for all three manufacturers were arguing for a year's delay in the 1975 standards, that they all painted pictures of economic disruption and wholesale closures if they were forced to introduce catalysts on all their cars next year. Now, however, not only is General Motors planning to introduce catalysts nationwide next year, but Ford is also planning to fit them to all their California cars and 65% of their others. Environmentalists have been quick to ask what happened to the dire forecasts.

As for the latest round in the battle, the arguments for delaying the standards have revolved around three chief questions—are the standards stricter than necessary simply to protect public health? Will the catalysts lead to another serious health problem, namely, the production of sulphuric acid from sulphur in petrol? And, finally, will they contribute to the energy crisis by decreasing engine efficiency? In each case, Ford and Chrysler argued that it would be sensible to delay implementing the standards until those questions have been answered. Clearly, if catalysts are installed next year and it subsequently turns out that they are not needed, several hundred million dollars will have been wasted.

The question of the standards being stricter than necessary is one on which the manufacturers are almost united, and they have also received direct and indirect support from the National Academy of Sciences for their arguments. In September, for example, Dr Arthur Stern, chairman of an NAS committee which has been looking into auto pollution, said that he believes the standards are three times stricter than necessary. That statement has, of course, been seized by the manufacturers and bandied about in committee rooms and Congressmen's offices ever since, but they are looking to the academy to provide even more support for their case next year. The academy has been given a contract by the Senate Public Works Committee to conduct a massive study of the health effects of pollutants, and the car manufacturers are convinced that when it reports next year, the academy will vindicate their own findings that the standards are much too strict.

In any case, the manufacturers have been arguing with some conviction that the 1975 interim standards should be delayed until the academy has produced its report, since, by next summer, catalysts will already be clamped to car exhausts and it will be too late to turn back if the study finds that they are not in fact needed. But the EPA, in the person of Mr Train, testified that relaxation of automobile controls next year would not only be a waste of money but

motor manufacturers efforts to clean up their products, but it would also cause many state governments grave problems in meeting other standards specified by the clean air act. He thus refused to entertain the idea of yet another delay.

As for the question of sulphuric acid emissions, that has already caused a split within the Environmental Protection Agency and raised some genuine fears that the catalyst may cause almost as many problems as it solves. The problem is the catalytic converters oxidise not only carbon monoxide and hydrocarbons to carbon dioxide and water, but they also oxidise some of the sulphur in gasoline to sulphur trioxide, and that could result in dangerous levels of sulphuric acid and sulphates in city air.

The problem first came to light earlier this year, and it prompted the EPA's director of research and development to suggest in an internal memorandum that the introduction of catalysts should be delayed until the problem has been given further study. According to the EPA's latest estimates, cars equipped with catalysts will spew between 3 and 5 times more sulphate into the atmosphere than cars not equipped with converters. Mr Train also stated at the hearings that EPA scientists have concluded that unless a mechanism is developed to control sulphate emissions, "more than one model year of cars equipped with catalysts could result in ambient levels of sulphates reaching levels at which recent studies suggest there will be adverse health effects". The EPA will soon be releasing a technical report on the matter, but in any case Train emphasises that if a problem does arise, there will be ample time to find a solution before there is a public health risk. Moreover, Mr Cole testified that "our (GM's) tests and atmospheric modelling show that while there may be some possibility, there is little probability that roadside atmospheric levels of sulphates from catalyst equipped vehicles by themselves will reach any threshold health levels".

But it is on the question of petrol consumption that General Motors testimony was most seriously out of line with that of the other two motor manufacturers. Until recently, all three car makers have been arguing that the exhaust catalyst will greatly increase fuel consumption, a fact that will not do much to help solve the energy crisis. But, much to the dismay of Ford and Chrysler, Mr Cole told the Senate committee that General Motors' cars equipped with catalysts to meet the 1975 emission standards will consume on average 13% less fuel than models being sold this year. To be sure, part of the reason for the dramatic drop is explained by the fact that GM, along with other manufacturers, will be pro-

ducing smaller cars, but the statement has clearly cut the ground from under Ford and Chrysler's attempts to ride the energy crisis bandwagon to put public opinion on their side in the battle against the catalyst.

Thus it seems inevitable that catalysts will be fitted to some 60% of all cars sold in the United States next year. But the debate will carry on for years to come.

ROYAL SOCIETY

Future Energy Sources

ENERGY in the 1980s, last week's symposium at the Royal Society, painted several different pictures of future trends. Mr D. Clark of the Central Electricity Generating Board, pointing out that his board is the largest consumer of fuel in Europe, stated that coal will be the board's staple fuel until the 1980s, when oil will become increasingly more important. The future after that will lie largely with nuclear power.

Up to the 1980s, Mr Clark said, the board can use all the coal that the National Coal Board can provide providing the price is right. But nuclear power will quickly become economical for lower load factors than at present. With forecasts based on a 5% growth rate, the year 2000 would see 24% of Britain's energy needs supplied by nuclear power. Towards the end of the 1980s, surplus nuclear generating capacity should be available on enough nights of the year to make energy storage a practicality.

But while coal still has a large part to play, Mr Clark was clearly not entirely happy at the prospect. "It is a fact", he said, "that over the last fifteen years electricity production has been hit a lot harder by stoppages in coal supplies than in oil supplies."

He also suggested that the volume of ordering of new coal-fired plant will be too small for technical innovations of any dramatic kind in coal plant.

Mr Leslie Grainger of the National Coal Board disagreed. By his calculations, the price of coal has virtually to double before nuclear power becomes competitive for low load generation. Advances in coal utilisation such as fluidised combustion, liquefaction and gasification were all put forward.

"The time has come", Mr Grainger said, "when we should increase the scale of this operation". A demonstration fluidised combustion plant should be built and a fluidised liquefaction plant producing 10 tons a day should be constructed (a half ton a day plant is already running). Coal is going to be very important on a world scale for many decades, Mr Grainger added, and will increasingly be used for conversion to other forms of energy.

Mr E. B. Walker of Gulf Oil Cor-

poration was also optimistic about energy conversion. His interests lay in converting tar sands, oil shales and coal. By 1985, he predicted, 3.75 million barrels of synthetic oil a day will be being produced in the USA. "This will reduce the United States demands on world supplies," he added, "and will therefore greatly strengthen the free world", although it is highly unlikely that any of the synthetics will be exported. Oil extracted with hot water from tar sands is already being produced at the rate of 50,000 barrels a day and Gulf plan to invest \$900 million in a plant that will produce more than twice that amount. Two tons of tar sand produce about one barrel of crude. About the same amount of shale also produce a barrel of oil. But production difficulties in the arid Rocky Mountains mean that there will be long lean times before this source produces large quantities of oil. The cost of these synthetic crudes lies between \$4 and \$7 a barrel at 1970 prices.

Sir Peter Kent, Chairman of the Natural Environment Research Council and a former exploration manager with British Petroleum, warned of the difficulties that have already occurred in bringing North Sea Oil ashore. Pipelines are being laid at twice the usual depth for offshore oil in a stormy stretch of sea and "delays may very well arise".

Happy Hundredth

SIR RICKARD CHRISTOPHERS is 100 next Tuesday, November 27.

He started his scientific career in 1898 as a member of the Malaria Commission, jointly appointed by the Royal Society and the Colonial Office. Ronald Ross had just published his classical work on the mosquito as vector and Christophers, with his deep understanding of insects, was able to exert an enormous influence on the study of diseases borne by mosquitoes. He worked largely in India until 1930 and then returned to London to continue at the London School of Hygiene and Tropical Medicine. On retirement in 1938, he moved to Cambridge and spent part of the war working on insect repellents. From his reports to the Malaria Committee (1900-02) to his 700-page volume *Aedes aegypti*—the Yellow Fever Mosquito (1960) his publications have been of the greatest distinction.

Sir Rickard finally moved to Dorset in 1963 where he spends much of his time gardening. A full tribute appears in *Trans. R. Soc. trop. Med. Hyg.*, 67, 729 (1973).

Short Notes

Population Dilemma

"We must reduce, halve and eventually reverse the present population growth rate." These were the words used in London on Wednesday by Mr Ron Dick, director of Population Countdown, at the start of the organisation's campaign for World Population Year.

Population Countdown aims to raise £150,000 during 1974—World Population Year. The money will be spent on supporting family planning projects throughout the world as well as on making the people of Britain aware of the world's growing population.

Between now and the end of the year Population Countdown will spend £12,000 on advertising in Britain. This money, Mr Dick said earlier this week, has come from a "special donor".

Less than 15% of the money collected by the organisation will go on overheads according to Mr Dick. The eventual aim of the campaign is to raise £1 million a year by 1977-78. During 1974 Mr Dick hopes to set up about 100 local groups throughout Britain to help with the appeal.

Population Countdown is a revamped version of an organisation set up by the Family Planning Association two years ago. In its old form the organisation was not too successful in raising money. But Mr Dick is confident that Population Countdown will meet its stated aims.

In the wake of the flood

THE *Financial Times* may have informed its readers in headline last week that the return of the horse is not the answer to Britain's energy crisis, but other organisations are not so bashful. The Inland Waterways Association has seized the chance of Arab oil embargoes to inform the government that its duty is to "consider methods of reducing our consumption of fuels without jeopardising our industrial viability. Transport, accounting for over one-fifth of our total energy consumption, offers the possibility of such economies". Quoting a 1972 report from Oak Ridge National Laboratory in the United States the association claims that waterways are four times more efficient than roads in terms of fuel consumption.

The Europeans are well aware of the advantages of water transport, the association says. "We ask that the Government, in the interest of fuel economy should update transport investment policy to include a realistic assessment of inland water transport on major new or enlarged waterways".

Less labour. less pollution. less noise.

less road congestion and lower freight rates are the advantages. Can the government refuse?

Indian-Soviet Collaboration

THE plans for launching an Indian research satellite by a Soviet rocket from a base within the Soviet Union are now past the first stage, according to Academician Boris N. Petrov, Chairman of the Interkosmos Council. The organisational basis for the joint project has been established, and the working plans completed. Now all that is necessary, it would seem, is for the satellite to be built.

According to Academician Petrov, "dynamic and static tests on a volume-weight mockup" of the satellite are now under way. The Soviets will provide the rocket—which will be similar to those used to launch the joint Comecon "Interkosmos" satellites. They are also assisting the Indian designers with certain auxiliary systems and elements for the satellite itself. According to the Indian director of the research team, the satellite is intended to monitor solar neutrons and gamma-rays, X-radiation of cosmic origin and also to investigate the ionosphere. Flight control and telemetry will be carried out from bases in both the Soviet Union and in India. The satellite is envisaged by the 200-strong Indian team as only the first step in an extensive space research programme, which will eventually cover applications to meteorology, communications, navigation and mineralogical surveying.

Law of the Sea

A FINAL date has been fixed for the full United Nations Law of the Sea conference that should resolve many questions about territorial waters, patrimonial seas, the law of the high sea, pollution matters and the freedom of oceanography. The conference will get under way on June 20, 1974, at Caracas in Venezuela and is due to last ten weeks. The venue has been changed from Santiago following the recent Chilean coup. The USSR, among other countries, was not prepared to go there.

Neanderthal Remains

EXCAVATIONS at the palaeolithic site of Belogorsk (Crimea) are yielding further Neanderthal remains. Last year, part of the skull of an 11-12 year old child was discovered; further excavations have now revealed a femur, a radius, several vertebrae, and hand and foot bones. Interviewed in *Pravda* (November 12, 1973), Professor Vsevolod P. Yakimov, Director of Moscow Univer-

sity's Institute of Anthropology, said that the new finds probably came from the same skeleton as the skull. On the basis of preliminary investigations at the Institute, he assigns the burial an age of some 50,000 years. Excavations at Belogorsk, which were begun in 1971 by the Academy of Sciences of the Ukrainian SSR, have also yielded mammoth, horse, fox and wolf bones, as well as flint implements.

Blessing Bessborough

THE Institution of Civil Engineers has decided that the Bessborough Report on the Research Associations is, by and large, a good one. The institution has sent its comments on the report to the government and particularly welcomes the proposal that a Board of Industrial Research and Development should be formed with a standing similar to the research councils.

The establishment of the board, the ICE says, would allow coordination over the wide areas of interest that the forty-odd research associations cover. Integration of this research with the research councils and the government research establishments should also be possible.

The institution does, however, sound several warning notes. Increased research and development in the construction field would produce benefits far greater than the extra cost while ocean engineering in particular needs support.

The institution is also eager—along with the Bessborough committee—that more contract research from industry should be placed with the research associations.

More Sandwiches

SANDWICH courses are to come under investigation by a working party set up by the Universities, Polytechnics and Industry Committee.

The setting up of this group has been precipitated by a feeling in industry and in the education world that the increase in training places is not keeping pace with the growth of sandwich course places in the further and higher education sectors.

The group will consider, in general terms, the value of the sandwich course scheme. It will also investigate the future development and expansion of courses, the concomitant need for increased provision of industrial training places, and finance and long term policy in this area.

Dr G. Tolley, Principal of Sheffield Polytechnic, will be the group's chairman.

NEWS AND VIEWS

Redshifts of Quasistellar Objects

THE physical nature of quasistellar objects is as puzzling now as it was 10 years ago when their large redshifts were discovered. Within 3 years of those first redshift determinations the difficulties encountered theoretically in explaining the observed radio and optical properties of the QSOs, if they were indeed at the enormous distances derived cosmologically, had been clearly laid out. Attempts were made to find alternative explanations for the redshifts, in terms of local objects exploding outward from our Galaxy at relativistic velocities, or collapsed objects whose radii had shrunk to near the Schwarzschild limit so that huge gravitational redshifts were present. But these theories were unsatisfactory either on energetic grounds or because of lack of a physically viable model of such an object near the limiting Schwarzschild radius.

A small minority of workers have maintained a sceptical attitude toward the hypothesis that the QSO redshifts are cosmological in origin, produced by the expansion of the Universe. These workers have mostly accepted that no viable alternative theory for the redshifts exists at present, and they have either pressed for additional observations along any lines that appeared promising for settling the controversy, or they have attempted to devise and carry out such observational programmes themselves, or they have made attempts toward devising alternative theories. But above all they have tried to persuade workers to keep an open mind on the question and, especially, not to ignore any data which pointed toward non-cosmological redshifts.

The large majority of astronomers, however, has adhered to the cosmological hypothesis, because this works well for normal galaxies, and because any alternative hypothesis would involve some radical new thinking.

Unfortunately, it has been very difficult to devise observational tests to give a conclusive answer, because most have had to be based mainly on statistical arguments, or on a painstaking and time-consuming search for luminous connections between objects of different redshifts. To collect enough data when time on large telescopes is in great demand is a real problem. The lack of precision in radio source positions has also led to a considerable amount of wasted telescope time.

It is therefore very interesting that astronomers seem at last to be within shooting distance of making some crucial tests. This has come about mainly because of the recent dramatic improvement in the accuracy of radio positions, so that errors are down to 2 arc s or better in some cases, through work at Molonglo, Cambridge, Malvern and Jodrell Bank, and other radio telescopes now starting precision work.

Two exciting pieces of optical work, made possible by these improved positions, are reported in this issue of *Nature*. The first concerns the discovery of a second double QSO with very discrepant redshifts (Wampler *et al.*, on page 203), a joint result by optical workers at Lick Observatory and Hazard on the radio side. The first pair of QSOs with discrepant redshifts, discovered some time ago by Stockton, were 35 arc s apart, but the new pair are at only 5 arc s separation. There is in

addition a faint extended object very near, and the radio source is double with one component coinciding with the brighter of the QSOs. Such a configuration is highly suggestive of physical connection. The authors conclude that "our observation of a close pair of QSOs with discordant redshifts is unlikely under the cosmological hypothesis" and "we believe that these observations add support to non-cosmological theories of redshifts". They also point out some interesting near-coincidences in wavelength: if the brighter and fainter QSOs are a and b , $(1+z)_b \approx 2(1+z)_a$; an absorption feature appears in b very near the wavelength at which strong MgII2800 emission occurs in a but it is probably the CIV1549 doublet at a lesser redshift than the emission-line redshift in b . Finally, there is an emission in a at the same wavelength as strong CIV emission in b . The authors conclude that these all represent "either an unfortunate coincidence or a profound mystery".

The second paper (Hazard *et al.*, on page 205) is joint work by radio and optical astronomers at Hale and Lick Observatories. With the improved radio positions, a search was made for close groupings of blue stellar objects coincident with a radio source and with three or more galaxies near the BSO. The important point is that it was not known during the search whether the BSOs were QSOs or, of course, what their redshifts were. Previous work in which QSOs had been found in close proximity to galaxies had been of two sorts. Burbidge *et al.* had found four (and later a fifth) 3C QSOs lying close to fairly bright galaxies of very different redshifts, a result which yielded high statistical significance, but this result concerned strong radio sources and bright galaxies.

Several other workers have looked for faint groups or clusters of galaxies near QSOs of small redshift. Since the QSO redshifts are known and selected in advance, and since galaxy groupings selected are in the right magnitude range to have redshifts of approximately the QSO value, the investigations, which yielded galaxy redshifts agreeing with the QSO redshifts, were of course clearly biased toward finding support for the cosmological redshift hypothesis, as Hazard *et al.* pointed out. Their investigation is unbiased, and the results are very interesting.

Of four sources selected for study, one was in fact the double QSO described earlier. But in all the other three cases, the fact that the BSO proved to be a QSO of large redshift, obviously much larger than those of the nearby galaxy groups as indicated by their magnitudes, is most intriguing.

The authors point out that no statistical conclusions can be drawn with so few samples, and conclude by leaving open the question of the nature of the redshifts. But one may at last hope for a resolution of the problem; because of the new accurate radio positions, optical observers can spend telescope time examining all BSOs near a radio source and even objects of neutral or reddish colour. In this reviewer's opinion, the case for non-

From Cyclic AMP to Cyclic GMP

CYCLIC AMP (3',5'-adenosine monophosphate) is now biochemical folklore and occupies the same hallowed position as its precursor, ATP (adenosine triphosphate). After a humble birth only 16 years ago, as a curiosity in Sutherland's work on the regulation by adrenaline of hepatic glycogen metabolism, by 1965 it was hailed as an almost universal 'second messenger' for hormones. Since then there has been no major biochemical regulatory event which has not been thought to be mediated by means of cyclic AMP (more than 2,000 papers, a dozen books on cyclic AMP this year and one more serial publication—*Recent Advances in Cyclic Nucleotide Research*—to add to the librarian's shopping list). Even if some of the hypotheses on the role of cyclic AMP are still questionable, this cyclic nucleotide has opened up new areas of research—phosphokinases and protein phosphorylation, gene activation in bacterial adaptation, cellular aggregation and slime mould differentiation, to quote only a few. What has attracted little attention during these past 5 or 10 years of intense activity are regulatory events in which cyclic AMP seems to have no part to play. Quite recently, however, a more interesting story than was imagined only a couple of years ago is emerging and this is where cyclic GMP (3',5'-guanosine monophosphate) comes in.

Already in 1969 Sutherland's laboratory had shown that cyclic GMP compound is present in urine and tissues of a variety of animals (Hardman *et al.*, *J. biol. Chem.*, **244**, 6354; 1969). It is interesting that tissues with relatively small concentrations of cyclic AMP, such as brain, testis and lung, are rich in cyclic GMP. Because of cyclic AMP's initial association with hormone research, the first indications that something important still lay concealed also arose from investigations on hormones. One can arbitrarily classify hormones into two categories: (1) those that act by controlling cyclic AMP activity in their target tissues, such as adrenaline, glucagon and almost all pituitary and hypothalamic polypeptide hormones; and (2) those that do not, such as steroid hormones, thyroid hormones, insulin and plant hormones.

It is studies on this second class of hormones that have yielded one of the clues to the involvement of cyclic GMP in biological regulation as, for example, the recent observation that insulin leads to increased activity of cyclic GMP in adipose and liver cells (Illiano *et al.*, *Proc. natn. Acad. Sci. U.S.A.*, **70**, 2443; 1973). Different groups of workers have also demonstrated that cyclic GMP when added to isolated tissues and cells has profound metabolic effects which could not be produced with cyclic AMP. Of particular importance are the findings of Greengard's group who showed that in lobster muscle and neuroblastoma cells there exist two quite distinct protein kinases—one dependent on cyclic AMP and the other on cyclic GMP (Kuo and Greengard, *J. biol. Chem.*, **245**, 2493; 1970). These workers, who have considerably advanced knowledge of the role of cyclic nucleotides in neural function, were also able to show that the cerebellum was particularly rich in a guanyl cyclase activity (conversion of GTP to cyclic GMP) and most tissues examined so far have now been shown to contain this enzyme. Several properties of this enzyme, not least its weak association with membranes, seem to be different from those of the classical membrane-bound adenylyl cyclase system which is

(Hardman and Sutherland, *J. biol. Chem.*, **244**, 6363; 1969).

As with progress in many other areas of biochemistry, the speed and accuracy with which a new concept can be tested often depend on how successfully analytical technology could be tailored to tackle new questions. This is true for cyclic GMP. The extremely small intracellular amounts of this nucleotide (10–100 fmol g⁻¹, or 10–50 times smaller than those of cyclic AMP) meant that, until recently, the assays were extremely laborious and often unreliable. The radioimmunoassay method (Steiner *et al.*, *Adv. Biochem. Psychopharmac.*, **3**, 89; 1970), now tried out in many laboratories, has, however, opened the way for eventually establishing cyclic GMP as an important intracellular mediator of metabolic and growth regulation, perhaps of the same importance as cyclic AMP.

Thus, thanks to a reliable assay for cyclic GMP, several interesting differences between the two cyclic nucleotides are now apparent. First, hormones like insulin, cholinergic (acetylcholine) or other agents (histamine) important in neural function, and lentil mitogens, all of which are known not to depend on cyclic AMP for their action, now seem to act by way of cyclic GMP. Second, it is becoming more and more apparent that there exist not only distinct cyclases, but also distinct phosphodiesterases and cyclic nucleotide binding proteins (or phosphokinases) which suggests that sites of synthesis, degradation and action are not the same for the two cyclic nucleotides. Perhaps of even greater interest is the suggestion that the high concentrations of one cyclic nucleotide prevent the formation, metabolism or action of the other. Evidence for this is not always firm or unanimously accepted; for example, the suggestion that cyclic GMP may cause a reduction of intracellular concentrations of cyclic AMP by activating the specific phosphodiesterase for cyclic AMP is disputed.

Whatever will be the more acceptable conclusion for the above particular phenomenon, Goldberg at the University of Minnesota has been fascinated by the mutual antagonism between the two cyclic nucleotides and has recently formulated an interesting hypothesis, in which he and his collaborators rationalise the diverse effects of these two key purine metabolites. In a review which is to appear in volume 3 of *Recent Advances in Cyclic Nucleotide Research*, Goldberg and his colleagues say that a signal such as a hormone or a neurotransmitter may exert 'monodirectional' control of generating either cyclic AMP or cyclic GMP, with each nucleotide having a separate stimulatory effect. It seems that all such 'monodirectional' systems (for example, the regulation of salivary gland secretion by parathyroid hormone) are for some reason calcium-dependent. Goldberg and his colleagues also offer a 'bi-directional' model of control embodied in the 'dualism' or Yin-Yang hypothesis, based on an analogy from the classical Chinese precept which states that for every point of stimulation (say, of a nerve, as in the practice of acupuncture) there is a corresponding point of inhibition or suppression. Thus in a bi-directional system, stimulation or inhibition of a process is achieved by a simultaneous drop in concentrations of cyclic AMP as those of cyclic GMP increase, and indeed this seems to be the case in a variety of systems that these workers have examined.

The dualism of Yin-Yang hypothesis is also supported

by observations that cyclic GMP promotes events in the cell that are antagonistic to those mediated by cyclic AMP. Conversely, artificially increasing the intracellular concentration of cyclic AMP, as with theophylline, led to an abolition of the response to cyclic GMP whether given exogenously or generated within the cell. These observations are not often easy to record because the changes in amounts of cyclic GMP are very low and transitory and because of a further variable, calcium, which is required for most cyclic GMP mediated effects. Nevertheless, in making these observations Goldberg and his associates have laid open for future experimentation many interesting regulatory systems. In a recent paper by Goldberg's group (Estensen *et al.*, *Nature*, **245**, 458; 1973) it is shown that movement of leukocytes, which is known to be inhibited by cyclic AMP, is markedly promoted by cyclic GMP. They propose that chemotactic agents like cytochalasin B, phorbol myristate acetate (PMA) or acetylcholine may act by potentiating the action or increasing the concentration of cyclic GMP. Furthermore, anybody dealing with such important phenomena as cell proliferation, viral transformation of cells, induction of immune response, action of nerve growth factor, in which cyclic AMP has an inhibitory effect, ought to examine a positive involvement of cyclic GMP.

It is, after all, not very long since interest in cyclic GMP has been gathering momentum so that many of the observations noted here still await rigorous confirmation. Among the more important issues that will soon have to be settled are:

- The location of guanyl cyclase. It is believed that adenylyl cyclase is situated within the close proximity of

the receptor for the hormone, or other biologically active agent; within the plasma membrane of animal cells. If guanyl cyclase turns out not to be a membrane enzyme, then it raises the interesting question of the nature of its association with the cellular receptor; particularly for molecules such as insulin which are currently thought to act from outside the cell.

- Mere changes in the intracellular concentration of cyclic GMP are not sufficient evidence of a primary regulatory role for this cyclic nucleotide. It is therefore urgent to identify cyclic GMP binding protein(s), and in this context the distinctness of protein kinases dependent on cyclic AMP and cyclic GMP offers a valuable clue. One has here only to consider how valuable the recognition of cyclic AMP binding protein has been to establish the role of cyclic AMP as a mediator of gene activation in *Escherichia coli* (Pastan and Perlman, *Adv. Cyclic Nucleotide Res.*, **1**, 11; 1972). There is also the subsidiary issue of clarifying the role taken by calcium in the action of cyclic GMP.

- The more general biological problem of key metabolites, or 'second messenger', a term first coined for cyclic AMP, that have to be generated for a regulatory agent to exert its action will have to be considered. Will it stop at cyclic GMP or will there be a flood of similar intermediate control elements? (At least the cyclic pyrimidine monophosphates seem to have been ruled out.)

Answers to all these questions may require some patience, but judging from the exponential rate at which publications are appearing, it will not be long before cyclic GMP is established as the second 'second messenger'.

J. R. T.

Immunopathology of Parasitic Infection

MOST parasites are capable of evoking immune responses in their hosts but these are seldom effective in eliminating the infection because parasites have evolved a number of ways of evading the immune response and its consequences. Some, like the African trypanosomes and malaria parasites, continually change their antigens and outwit the immune response in this way. Others, like the schistosomes, incorporate host material into their surfaces and thus become immunologically invisible. A major problem in many parasitic diseases is that not only is the immune response ineffective but it may also give rise to a variety of pathological conditions. The immune response may therefore be counterproductive. Glomerulonephritis is a serious consequence of both African sleeping sickness and malaria and is thought to be initiated by the deposition of antibody-antigen complexes in the kidneys. The localised immune responses evoked to deal with these complexes have no effective role in protection. The parasites continue to multiply elsewhere in the body and soluble antigens pass into the circulation to give rise to the antibody-antigen complexes in the glomeruli.

The problems brought about by an immune response which takes place away from the site of infection also occur in schistosomiasis. The adult worms live in mesenteric blood vessels and their numbers are controlled by an immune response which has been completely manipulated by the parasite. The worm takes up host antigens from the blood and incorporates them into its

surface. Sheathed in host antigens, the worm is immunologically invisible but continues to pass antigens into the blood stream to elicit an immune response which is effective only against new invading forms as they migrate through the skin and underlying tissues of the host. This kind of response should produce a well balanced host-parasite relationship and prevent overcrowding of the worms. Crofton (*Parasitology*, **62**, 179; 1971) has pointed out that helminth infections tend to be overdispersed and most hosts harbour relatively small and easily tolerated worm burdens. In such circumstances only the very heavily infected hosts would be expected to die and most would not be unduly inconvenienced by the infection.

Unfortunately there is a major complication in schistosome infections. The female worms release large numbers of eggs which enter the blood stream and lodge in the small blood vessels in a variety of tissues especially the spleen, lungs and liver where up to 10,000 per gram may be found. These eggs cause granulomas to form. The granulomas begin as reactions involving macrophages, lymphocytes and eosinophils and later become fibrous. The formation of granulomas eventually leads to liver obstruction and liver function failure and, in experimentally infected animals, the liver may reach double its normal size. The granulomas are obviously very important in the pathology of schistosomiasis.

For many years it was widely held that the granulomas were the result of a cellular response to irritation but it is now known that their origin is immunological. This

realisation has gradually emerged from a carefully directed research programme extending over 16 years by K. S. Warren of the Case Western Reserve School of Medicine and a number of collaborators. Warren has summarised the evidence that granuloma formation results from a delayed hypersensitivity reaction (*Trans. roy. Soc. Trop. Med. Hyg.*, **66**, 417; 1972) and has since extended these findings with the collaboration of D. L. Boros who originally joined him as a post-doctoral research worker. On page 224 of this issue they describe how they, and Pelley, have isolated granulomas *in vitro* and have extracted from antigen stimulated granulomas a substance that inhibits the migration of macrophages and which they identify as a lymphokine. In another paper Boros and Warren (*Immunology*, **24**, 511; 1973) describe how the intravenous injection of bentonite particles impregnated with the antigen elicits granuloma formation in the lungs of sensitised mice.

The antigen is a soluble substance released from the egg. After the egg is laid embryonation occurs and this is accompanied by the liberation of enzymes and soluble antigens (which may be enzymes). The egg acts as a focus for the granuloma. Macrophages enter the immediate vicinity of the egg and come under the influence of the lymphokine and are unable to move away. In most bacterial and fungal infections this kind of local reaction isolates the invading organisms which are then phagocytosed by the macrophages. In schistosomiasis, however, a granuloma 100 times the size of the egg is formed and this is gradually replaced by fibrous scar tissue. Boros and Warren have also found that bentonite particles impregnated with mycobacterial and histoplasma antigens induce granulomas in animals sensitised with homologous antigens but not heterologous ones.

It is clear from these experiments that the pathology of schistosomiasis is not unique and comparable situations probably exist in a number of parasitic infections. The existence of non-protective delayed hypersensitivity states in parasitic diseases makes vaccination attempts potentially dangerous procedures which might even lead to immunological enhancement. The World Health Organisation (*Tech. Rep. Ser.*, No. 519, *Cell Mediated Immunity and Resistance to Infection*; 1973) is fully aware of this problem and as more information about

immunity to parasitic diseases accumulates the possibilities of developing useful methods of immunisation fade further and further into the distance.

F. E. G. C.

CONTRACEPTION

How Safe is Safe?

from a Correspondent

How safe is the 'safe' period as a means of contraception? This will depend among other things upon how long the ovum and sperm can exist in the reproductive tract without loss of the ability for fertilisation and how fixed in the menstrual cycle is the time of ovulation. Can ovulation in normally menstruating women occur at times other than at about mid-cycle? Can it be induced, or can spontaneous ovulation be hastened, by coitus? Although coitus-induced ovulation occurs in many species it is not usually considered to be a phenomenon in humans.

Jöchle (*Contraception*, **7**, 523; 1973) has now reviewed the evidence relating to this question. The length of the luteal phase of the cycle seems to be fairly fixed at about 14 days; variations

in menstrual cycle length usually result therefore from variability of the follicular phase. It is known that hypothalamic-pituitary-ovarian function can be modified by environmental change resulting in inhibition of ovulation and a consequent change of menstrual pattern or the complete absence of menstruation (psychogenic amenorrhoea).

The possibility exists therefore that other environmental changes might stimulate pituitary gonadotrophin secretion and produce ovulation. That ovulation can occur at times other than mid-cycle has been suggested by examination at autopsy of ovaries and uterus and calculation of the time interval in which ovulation must have occurred. When this interval was related to the time of menstruation of the previous cycle the results suggested that ovulation could occur at any time in the cycle. Similar observations made at surgical operations also suggested that ovulation could occur on any day of the first half of the cycle.

Evidence in support of coitus-induced ovulation was obtained from two sources. (1) Conceptions resulting from rape, using data only from patients for whom reliable information could be

Haemin Selectively Stimulates α Globin Synthesis

THE study of the role of haemin in protein synthesis is interesting because it provides evidence that some regulation takes place at the level of translation. When haemin is added to a cell-free system containing globin messenger RNA globin synthesis is stimulated, but so too is the synthesis of endogenous proteins. By contrast, when its effect is studied in an *in vitro* system (for example, when globin mRNA is injected into *Xenopus* oocytes), only the synthesis of globin is increased.

In *Nature New Biology* next Wednesday (November 28) Giglioni *et al.* describe some experiments designed to help elucidate the function of haemin in globin synthesis. Using the oocyte system they have found that in conditions of rabbit globin mRNA saturation there is about four times more β globin than α globin synthesised. By increasing the amount of haemin added to the system α globin synthesis is proportionally increased until a haemin concentration of 30 μ M when the ratio remains constant with α globin nearly 40% of the total globin synthesised in the system.

Endogenous protein synthesis is unaffected even at high haemin concentrations. At subsaturating levels of mRNA an $\alpha:\beta$ globin ratio of 1:1 can be achieved by injecting haemin into the oocytes, and if globin mRNA rich in α messenger is used more α than β is

From these results alone, the possibility cannot be excluded that haemin affects the recovery of the globin chains, after their release from the ribosome, rather than their synthesis. The results of control experiments, however, make the first suggestion extremely unlikely. Control experiments also exclude the possibility that the low α to β ratio, in the absence of haemin, is due to a delay in the release of α chains relative to β chains.

It seems clear that in this system haemin controls the synthesis of α but not β mRNA. The authors suggest that the mRNAs for α and β globin compete for some component necessary for their translation (but not that of endogenous mRNAs), and that the effect of haemin is restricted as soon as mRNA concentration becomes saturating.

It is difficult to know how far these results can be extrapolated to explain the action of haemin in intact reticulocytes. If reticulocyte-rich blood is incubated in the presence of lead the synthesis of haemin is inhibited and this is followed by a 90% reduction in globin synthesis. The absence of haemin in the oocyte system does not have such a depressing effect. In haemin-free reticulocytes, however, the α globin synthesis is inhibited more than that of β globin so that in this important aspect the oocyte system and reticulocytes are

obtained about the menstrual cycle, its pattern and time of the last menstruation before rape. Analysis of these conceptions showed that 33–46% of all conceptions took place during the safe period after menstruation, 10–30% during the safe period before menstruation and about 8% during menstruation itself. Thus fertility seemed to be elevated during most of the first half of the cycle and not only at about mid-cycle. (2) Conceptions resulting from limited exposure. An evaluation of 100 carefully selected cases showed that the risk of conception during the first and last four-day period of the menstrual cycle could be as high at 10% of the risk of conceiving during the mid-cycle period. In an investigation involving 241 British women who were using the basal body temperature method for birth regulation and who were studied throughout nearly 2,000 cycles, the conception risk was highest between days 10 and 12 of the cycle. The risk, however, was still very high at any time from day 5 to day 15 and, although markedly reduced during the luteal phase, the risk could still be up to 5%.

The value of this type of evidence depends on the surety that no other cohabitations took place during the period in question. Conceptions occurring in women with amenorrhoea have also been reported, although such evidence is difficult to evaluate in view of the possible spontaneous ovulation which occurs occasionally in these subjects.

Jöchle, after reviewing the evidence, concludes "the possibility of coitus-induced ovulation in humans should no longer be denied" and consequently it makes one sceptical whether the rhythm method of contraception can ever be completely successful. Most of the evidence quoted, however, is circumstantial; much less doubtful evidence is required before coitus-induced ovulation can be accepted as a reality.

PROTEIN SYNTHESIS

Ribosome Attachment

from a Correspondent

JOAN ARGETSINGER STEITZ has continued her studies on the control of the initiation of protein synthesis in the small RNA bacteriophage called R17. She had previously determined the nucleotide sequence of the three initiator fragments of the RNA, each about thirty residues long, which are responsible for the attachment of the RNA to the ribosome of the infected cell. These three fragments correspond to the three proteins, the coat protein, the replicase protein and the A protein, synthesised by the RNA.

She has now studied the interaction of

fragments rather than the intact 3,300-residue long RNA molecule, with ribosomes (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 2605; 1973.) Surprisingly, only the initiator fragment for the A protein has the ability to bind *in vitro* to either *Escherichia coli* or *Bacillus stearothermophilus* ribosomes. By contrast, the initiator fragments for the coat and replicase protein do not bind significantly. She concludes that the RNA ribosome binding site of the A protein seems intrinsically to be a good initiator, whereas efficient recognition of the short coat and replicase regions requires the participation of some portions of the remainder of the phage RNA molecule.

Steitz suggests in a discussion that the influence of these other parts of the RNA on the specific initiator regions is probably exerted by a control of the exact three-dimensional structure of the binding sites. The inability of the coat protein site to bind, however, was surprising as it is known to form a stable hairpin-looped secondary structure with an A-U-G codon (specifying the first amino acid, formyl methionine, of the coat protein) exposed in the loop. Presumably therefore this loop formation cannot be sufficient for recognition by ribosomes. In fact, as such a stable hairpin-looped structure is unlikely to be present for the A protein site in either the fragment or the intact molecule, Steitz suggests that the function of

the remainder of the R17 RNA molecule may actually be to facilitate opening of looped structures during ribosome attachment.

INSECT PHYSIOLOGY

Juice Extractor

from our Insect Physiology Correspondent

SINCE Léon Dufour in 1833 published his observations on the anatomy of the gut in the Homoptera, it has been known that most members of this group of plant-sucking bugs have a more or less complicated association between the commencement of the midgut and its termination, in conjunction with the Malpighian tubules, in the ileum (the first segment of the hindgut). Dufour named this arrangement the 'filter chamber' in which, as he supposed, the copious watery contents of the plant juices were filtered off directly to the hindgut, while the nutrient material was carried on to the midgut. But there have been no experimental studies carried out to substantiate this idea.

A physiological study of the kind required has now been made by Cheung and Marshall (*J. Insect Physiol.*, **19**, 1801; 1973) on a variety of cicadas in Hong Kong and Australia. Cicadas feed on xylem fluid which is hypotonic to the haemolymph of the insect and contains high concentrations of potas-

Soft Gamma-ray Bursts from Compact Objects

THE energetic soft γ -ray bursts observed by the Vela satellites could result from fleeting episodes of accretion on to nearby compact objects—neutron stars or black holes. The sixteen or so bursts seen so far last typically for 1 to 10 s and show significant structure on time scales as short as 100 ms. The uniform distribution of possible source locations over the sky suggests that the sources are local.

Taking the typical distance as 100 pc, the luminosity during each burst is about 10^{37} erg s⁻¹, with the radiation spectrum peaking at around 100 to 400 keV. In *Nature Physical Science* next Monday (November 26) Lamb, Lamb and Pines emphasise that these time scales and luminosities are characteristic of the compact galactic X-ray sources, which are thought to be neutron stars or black holes continuously accreting matter from their close stellar companions.

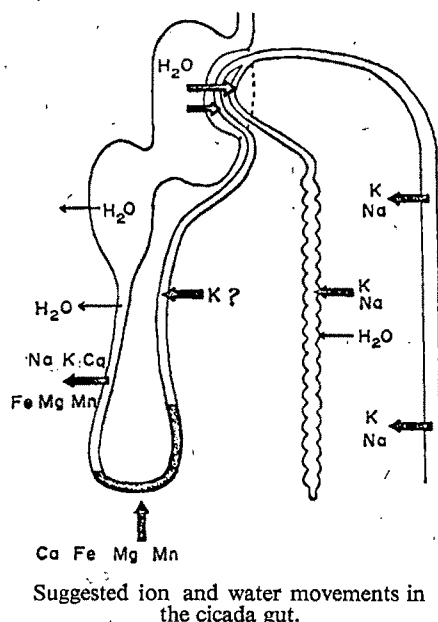
The space density of these X-ray sources is less than 10^{-8} pc⁻³. The authors, however, estimate the sources of the γ -ray bursts to have a space density of about 2.5×10^{-2} pc⁻³ and argue that the space density of binary systems containing a compact object

The amount of matter that has to be accreted in order to liberate the required amount of energy per burst is about 10^{16} g. The largest solar flares, occurring every 5 to 20 yr, eject a mass of about 10^{16} g at a speed of about 1,500 km s⁻¹. Thus if the binary companion of the compact object undergoes similar flaring activity—perhaps on a slightly larger scale, but not necessarily as violently as flare stars—accretion of a part of this ejected material can neatly account for the observed properties of the soft γ -ray bursts. Since the ejection velocity is so supersonic, the accreted material need have little angular momentum with respect to the compact object, and so is able to fall straight on to the surface without having to go through the relatively slow process of forming an accretion disk.

In ordinary X-ray sources with temperatures corresponding to about 10 keV, the energy liberated by the continuously infalling material is more or less thermalised on the surface. It seems plausible that the energy liberated by a single blob of matter falling on to the surface will be less completely thermalised and will, therefore, be radiated at the higher temperature corres-

sium, sodium, calcium, magnesium, chloride and phosphate ions. The urine contains the same ions in slightly lower concentrations. Amino acids and sucrose are present, and traces of amino acids persist in the urine. If xylem fluid is injected into the oesophagus there is an immediate ten-fold increase in the flow of liquid in the ileum. Meanwhile the osmotic pressure in the xylem fluid within the filter chamber rises, while the osmotic pressure in the anterior part of the ileum rapidly falls.

As the residual fluid passes on down the midgut, water, nutrients and ions are absorbed into the haemolymph and divalent ions are stored in granular form in the walls of the mid-midgut. Ions may be transferred from the haemolymph into the posterior tubular midgut, where the osmotic pressure of the contents is high in the post-feeding stage. Certainly the Malpighian tubules secrete a fluid which is rich in potassium (42 mM/l) and sodium (15 mM/l) and is hypertonic to the blood. Thus when the contents of the terminal midgut and of the Malpighian tubules reach the filter chamber and become intimately associated with its walls, they have an osmotic pressure considerably higher than that of the xylem fluid as it enters the filter chamber proper. Passive osmosis will therefore occur and water will thus be carried across the walls into the commencement of the ileum. Potassium and to a lesser extent sodium, as in other insects, are actively reabsorbed in the lower segments of the ileum and thus provide the recirculating ions needed to keep the machine going.



These results strongly suggest that Dufour was right and the chamber really is a 'filter chamber', and that the ionic concentrations needed to sustain its operation are the result of secretory activity elsewhere in the Malpighian

SILICA

Light Thrown on Charge Transport

from our Solid State Physics Correspondent

THE observation of currents in insulators has always been a difficult task and thus it is only recently that it has been confidently asserted that electrons travelling in solids with wide band gaps do so according to roughly the same laws as those in semiconductors, and that, given the necessary boost, electrons in solid dielectrics can be raised from the valence states to a conduction band and, in the right material, can then move easily and without undue scattering or trapping over large distances. Such evidence can only be gained by the use of high energy sources of light or particles and, preferably, very short pulses. Spear (see, for example, *Phys. Rev. Lett.*, **25**, 509; 1970) pioneered this work, deducing drift mobilities for electrons in such materials as Pyrex glass. From his technique, however, it was not easy to deduce basic quantities such as carrier lifetime and trapping frequency. Recently, Hughes (*Phys. Rev. Lett.*, **30**, 1333; 1973, and *Proc. Twenty-seventh A. Symp. Frequency Control, Cherry Hill, New Jersey*; June 1973) has greatly reduced the time scale by using very sharp X-ray pulses lasting only a few nanoseconds together with equally fast signal-recording techniques. So, for the first time, a carrier lifetime for silica has been obtained and an interesting array of effects has been revealed.

Application

These experiments are illuminating and important because silica is a particularly useful material both in the research and technological sense. The structure of silica, in crystalline and amorphous forms, has been intensively examined by diffraction techniques and the Si-O bond as a chemical entity is also much studied by organosilicon chemists. Silica is of great importance in technology—its uses range from rugged, expansion-free optics to crystal oscillators; further, silica has recently found new and important uses as a key element in metal-oxide-silicon devices, surface acoustic wave devices, optical waveguides and pressure gauges. Also, being a refractory, insulating material, silica may play a significant part in the building of a nuclear fusion reactor and indeed already provides the most long lived thermal protection for space vehicles exposed to intense radiation in space. The combination of strong piezoelectric response, optical transmission and controlled transport properties may also give silica an important place in optical integrated circuits. Thus, it is important to learn as much as possible about how charges and ions move in this material.

dioxide in thin-film form has been determined to be about 9 eV. It is known that intrinsic d.c. photoconductivity can be induced in the material and that the mobility of electrons is high, by contrast with that of holes which is much lower. The electron mobility in thin-film silicon dioxide is of the order $30 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ (Williams, *Phys. Rev.*, **140**, A569; 1965). This is a very high value for an amorphous material since Mott (*Adv. Phys.*, **16**, 49; 1957) estimates that a typical electron mobility for amorphous materials is about $1 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$. Thus, there is the extra interest of a new measurement of charge transport in a bulk solid—that it may at least confirm or contradict this surprising measurement and, furthermore, allow the measurement to be done on both crystalline and amorphous forms, a comparison not possible with thin-film silica.

A very high peak dose rate of X rays must be used, since, even with, say, $10^{10} \text{ rad s}^{-1}$ of 600 keV photons, the transient currents generated are small (of the order of a few nanoamps) and flow for a very short time (of the order of 10 nanoseconds). These measurements are, however, well within the bounds of the capabilities of Sandia Laboratories. Sandia is, in fact, interested in the possibly catastrophic effect of electric fields that are high enough to produce breakdown in quartz crystal oscillators or pressure gauges. Hughes has been able to distinguish between two forms of decaying current after the X-ray pulse and to distinguish cases in which the drift mobility is field dependent and others in which it is not. This is vital information, since the former condition indicates that many carriers are managing to transit the sample without being trapped, whereas the latter case indicates trap modulation in some samples, from the characteristics of which a carrier lifetime can be deduced. There is also a long lived component of the photocurrent which could represent an important check on a recent theory of radiation-induced ion mobilisation (McCaughan and Murphy, *IEEE Trans. nucl. Sci.*, **NS19**, 249; 1972). The most satisfying result is for very pure amorphous fused silica. As with the thin-film samples already mentioned, Hughes finds the carrier mobility in a bulk fused silica slab to be about $20 \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ at room temperature, increasing at lower temperatures to a saturation level of about 40. Not only does this fit well with the thin-film data but also with a theoretical prediction of Lynch (*J. appl. Phys.*, **43**, 3274; 1972) in which the temperature dependence is determined by longitudinal optical (LO) phonon scattering alone and predicts $32 \text{ cm}^2 \text{ V}^{-1}$

also correctly predicts the breakdown strength of silicon dioxide films—another indication that these measurements should rapidly find practical application.

Mobility and Lifetime

Surprisingly, mobility and lifetime are lower in crystalline silica and, although it is difficult to control the incorporation of impurities during the growth of quartz crystals, a correlation of carrier lifetime and mobility with degree of impurity of crystal seems to exist. For example, Hughes finds that lithium-doped synthetic quartz has a higher mobility-lifetime product than the non-doped variety, whereas the synthetic fused silica samples, always much more pure than the flux-grown crystals, typically have twice the carrier lifetime of the crystals and well over twenty times the mobility value. Although the reduced mobility might suggest trapping phenomena as the cause, the mobility exhibits little temperature dependence. Thus, the more likely explanation is some form of impurity scattering, as confirmed in semiconductors. The field dependence of the radiation-induced conductivity again suggests LO phonon interaction as the limiting effect, since the drift velocity saturates at about the levels predicted by Thornber and Feynman (*Phys. Rev.*, **B1**, 4099; 1970), around 10^7 cm s⁻¹.

The question, then, is why an amorphous solid should possess such high mobility—indicating a mean free path of about 40 Å—when, according to most theories of the amorphous state, the mean free path should be of atomic dimensions, on account of the presence of localised states induced by the presence of disorder (see, for example, the studies on amorphous silicon by Spear and Le Comber, *J. Non-cryst. Solids*, **8-10**, 727; 1972). This would seem to confirm the X-ray evidence (Konnert, Karle and Ferguson, *Science*, **N.Y.**, **179**, 177; 1973) that the short-range order in fused silica is very good, the only deviation from order being some variation in Si-O-Si bond angles. This probably means that there is not a large amount of bond strain in the atomic network, therefore the same wide distribution in binding energies found in many amorphous solids does not exist. This could well lead to a major reduction of the 'tail' of localised states normally required to explain the transport and optical properties of compounds like the chalcogenide glasses.

Certainly, the reflectance spectra of fused silica and quartz look astonishingly alike (Phillipp, *J. Phys. Chem. Solids*, **32**, 1935; 1971) and some might say that the high mobility suggests that silica borders on the microcrystalline. But just as melting produces no strong

conductors (see, for example, Adler, *Crit. Rev. solid state Sci.*, **2**, 317; 1971), it may be that electron transport continues to be efficient whenever short range order persists and thus so far the picture of fused silica as an amorphous solid remains. It should also be said that Hughes finds that holes seem to be very firmly lattice trapped and do not contribute at all to the photoconduction. This confirms most previous findings in thin-film silica and lends support to the current theories of space-charge build-up in these materials (see, for example, Zaininger and Holmes-Siedle, *RCA Rev.*, **28** (2), 208; 1967).

Implications

One general conclusion is that it may take as much (or more) trouble and time to obtain insulator crystals free of troublesome impurities as it did for semiconductors especially since, at the moment, there is not as strong a technological motivation for producing them. For those concerned with controlling radiation-induced conductivity (reactor designers and so on) manipulation of impurity scattering may, however, provide a useful tool for reducing unwanted conductivity. Second, one can echo a conclusion of Revesz (*J. Non-cryst. Solids*, **7**, 435; 1972) that the amorphous oxides, nitrides and related glasses might provide a good medium for the basic

study of the amorphous state because they are disordered only in the mildest way possible. Third, low field conduction work has received encouragement from these findings, which have tied together and strengthened some previously intriguing but hardly demonstrable hypotheses on transport in insulators and, incidentally, have annihilated at least one earlier theory of field dependence of mobility in silica (Onnasch, *Phys. stat. sol.*, **38**, 579; 1970).

PALAEONTOLOGY

Fossil Diversity

from a Correspondent

It is widely acknowledged that plate tectonics has had a revitalising effect on many fields of earth science, and nowhere is this more true than in palaeobiogeography, which is the name given to the study of fossil distributions in time and space. Abundant evidence of the burgeoning interest in this subject is provided by the numerous papers recently published in the *Atlas of Palaeobiogeography* (edit. by A. Hallam, Elsevier, 1973), and in two conference symposia, *Organisms and Continents Through Time* (edit. by N. F. Hughes, *Paleont. Ass. Spec. Paper* 12, 1973) and *Implications of Continental Drift to the Earth Sciences*, vol. 1 (edit. by D. H.

Rock of Grenville Age found on Rockall Bank

GEOPHYSICAL evidence suggests that the Rockall Plateau (and thus the Rockall Bank which forms part of it) may be a microcontinent isolated during one of the phases of spreading in the North Atlantic region. Until recently, however, geological evidence for a continental basement structure in the form of granitic or metamorphic rocks on the plateau was not entirely convincing, because, although several dredge hauls had been carried out in the vicinity of the plateau, most of the recovered samples could not be interpreted unambiguously. Moreover, further ambiguity was introduced by the presence of iceberg plough marks around the Rockall bank and evidence of ice-rafted deposition.

This equivocal situation was resolved earlier this year when Roberts *et al.* (*Nature phys. Sci.*, **244**, 21; 1973) reported the results of drilling two outcrops about 100 km apart in the southern section of the Rockall Bank. Granulite facies metamorphic rocks were found at both sites. In one case the hornblende in the drill core (acid granulite) was dated at 1566 ± 33 million years (Loxfordian) and the whole rock at 1670 ± 24 m.y. Thus the presence of continental rocks underlying the Rockall

tension, that the whole Rockall Plateau may indeed be a microcontinent.

But Roberts and his colleagues also proposed that rocks of Grenville age may occur on the southern section of the Rockall Bank—a prediction arrived at by considering the pre-drift reconstruction of the North Atlantic Ocean in the light of the new Loxfordian age. This prediction has now been confirmed by Miller, Roberts and Matthews who report their discovery in *Nature Physical Science* next Monday (November 26). The rock concerned, an andesine-orthopyroxene-biotite-quartz granulite, is that obtained previously by Roberts and his colleagues at the southernmost of their two sites on the southern section of the Rockall Bank.

This age obtained (987 ± 5 m.y.) is the first Grenville age found within the British Isles or west of the Caledonian Front in Europe and suggests that the Grenville Front crosses the southern section of the Rockall Bank, although confirmatory results from other rock samples will be required before certainty can be claimed. In the meantime, however, Miller and his colleagues make a further prediction—that rocks of Grenville age may also underlie parts of the Porcupine Bank or the continental shelf

Tarling and S. K. Runcorn, Academic, 1973). Most of these articles are concerned with patterns of organic provinciality or cosmopolitanism in relation to migrating continents. Another fruitful line of approach, however, has been to consider how fossil diversity, or taxonomic variety, might have been affected by plate movements in the past 600 million years.

Pioneer work in analysing diversity changes through Phanerozoic time in fossil marine invertebrates has been undertaken by the American palaeontologist J. W. Valentine. In a series of stimulating papers during the past few years, he has put forward interpretative models which attempt to relate the diversity patterns recognised to changing configurations of continent and ocean, and changing climate. A particularly commendable feature of his work has been the successful application of modern ecological concepts such as environmental stability to the fossil record.

Valentine recognises a rapid rise in the number of families and genera in the Cambrian and early Ordovician, reaching a maximum in the Devonian, followed by a progressive decline to a minimum in the late Permian and early Triassic. Subsequently diversity

seems to have increased at a high rate through the remainder of the Mesozoic and Cainozoic. The Palaeozoic and Cainozoic provinciality patterns are held to be quite different. During the Palaeozoic the existence of a huge supercontinent, and hence low environmental stability, centred around the South Pole favoured high climatic continentality and a mild thermal pattern of relatively low provinciality, also helping to limit diversity. In the Cainozoic high provinciality (and hence diversity) developed as a consequence both of dispersion of continental masses and stronger latitudinal differentiation of climate. The sharp drop in diversity at the end of the Palaeozoic is attributed to widespread extinction resulting from the creation of the supercontinent of Pangaea, by the suturing of several smaller continents, which led to increased interfaunal competition and to increased seasonal contrasts in climate.

Diversity changes through time can be considered in terms of secular trends and shorter-term oscillations. With regard to the former, Raup (*Science*, N.Y., 177, 1065; 1972) has questioned the pattern of changes outlined by Valentine by drawing attention to several possible time-dependent biases in the data.

To take one example, the chances of given fossil taxa being preserved will depend to a large extent on the chances of their containing sediment not being subject to erosion or metamorphism. Quite simply, these chances increase with decreasing age, hence the sharp and progressive diversity increase in the Mesozoic and Cainozoic could be an artefact, as could the late Palaeozoic diversity reduction, which seems to correlate well with a reduction of volume of marine sediment deposited at that time. Raup proposes an alternative model in which a mid-Palaeozoic diversity maximum is assumed, followed by reduction to an equilibrium level. He has generated a computer model on this basis, with the hypothetical diversity being modified by selective fossil destruction, the probability of which has been calculated to decrease through the course of time.

Raup is probably correct in claiming that Palaeozoic diversities were relatively higher than appear from Valentine's data, and that the strong post-Triassic increase may to some extent be an artefact. Since, by general consent, the end of the Palaeozoic marked a time of mass extinction with its obvious concomitant of reduced diversity, one must react more sceptically to Raup's postulated correlation with reduced marine sediment volume, which may be controlled by the same fundamental cause or be merely coincidental. His criticisms have less bearing, moreover, on the interesting and comprehensive work of Flessa and Imbrie (in the Tarling and Runcorn volume), which is concerned not with secular trends but with oscillations in diversity at intervals of 10 million years.

Flessa and Imbrie apply Q-mode factor analysis to rates of increase and decrease of many fossil invertebrate and vertebrate families, the fluctuations in numbers being treated as a function of rates of origination and extinction. Their analysis confirms earlier, less quantitative notions that the fluctuations of different groups are not random but tend to coincide in time. The conclusion is drawn that correlation with events associated with lithospheric plate movements is sufficiently good to suggest a significant relationship. Flessa and Imbrie go on to develop a predictive model for changing continent-ocean relationships based on the ecologists' well-known species-area equation. Graphs are produced showing the changes in diversity to be expected for a given change of continental area and differing degrees of cosmopolitanism and geographic isolation. In spite of the speculative nature of the exercise and the simplifying assumptions made, their analysis is very enlightening and suggests a promis-

SELENOLOGY

Near-surface Model

from our Geomagnetism Correspondent

ESTIMATES of the physical properties of the near-surface material of the Moon were made even in the days when the only data available were measurements of the brightness temperature of the lunar surface. Thus, for example, Piddington and Minnett (*Aust. J. scient. Res.*, 2A, 643; 1949) proposed that the lunar surface comprises a thin (about 1 mm) layer of fine powder covering a more solid base. Jaeger (*Aust. J. Phys.*, 6, 10; 1953) also concluded that the lunar surface is a fine evacuated powder, or at least acts like one thermally, to which Muncey (*Aust. J. Phys.*, 16, 24; 1962) added a high conductivity substrate. A few years later, Linsky (*Icarus*, 5, 606; 1966) suggested that the thermal conductivity in the upper few centimetres may be significantly temperature dependent.

So how do these older, pre-Apollo conclusions compare with those based on newer, more comprehensive measurements *in situ*? Keihm *et al.* (*Earth planet. Sci. Lett.*, 19, 337; 1973) have now combined *in situ* measurements of lunar surface brightness temperatures at the Apollo 15 Hadley Rille landing site, data from five thermocouples lying on or just above the surface at the same site and a density profile and a heat

Apollo data, to produce a model of the upper few tens of centimetres of the lunar regolith having the following characteristics.

The upper layer of the surface is about 2 cm thick and is strongly insulating, having a mean thermal conductivity in the range $0.9\text{--}1.6 \times 10^{-5} \text{ W cm}^{-1} \text{ K}^{-1}$ (*sic*). Below this surface layer there is a large conductivity gradient, resulting in a mean conductivity of $5.5 \times 10^{-5} \text{ W cm}^{-1} \text{ K}^{-1}$ at 5 cm depth; but at greater depths the conductivity increases more gradually to $1.4 \times 10^{-4} \text{ W cm}^{-1} \text{ K}^{-1}$ at 49 cm. In the upper few centimetres the conductivity is also strongly temperature dependent, and about 70% of the heat transfer at the highest temperatures is by radiation between particles.

The temperature dependent conductivity close to the surface is required to explain an observed high temperature gradient (an increase of 47 K in the upper 83 cm) and indicates the presence of very loosely packed material in the upper few centimetres. Since the particle configuration and degree of compaction in such material will be difficult to maintain once the material is moved, Keihm and his colleagues conclude that measurements made on returned lunar samples may indicate properties significantly different from those of the undisturbed lunar surface. This may be why their ratio of radiative to conductive heat transfer (at 350 K), for example, is almost twice that measured

Submillimetre Astronomy

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Although astronomy at submillimetre wavelengths is still in its infancy, work in two different areas—observations of HII regions and molecular clouds, and observations of the temperature minimum in the solar atmosphere—is particularly advanced.

NEARLY two decades of the electromagnetic spectrum from 20 μm to 1 mm have been virtually inaccessible to the astronomer because of severe absorption by the Earth's atmosphere. This spectral region is of great interest, however, from observations of the 3 K background radiation on the cosmological scale, to observations of star formation on the galactic scale, and the atmospheres of the Sun and planets locally. Recently, the submillimetre region has begun to be explored using balloons, rockets and aircraft as observing platforms, and from ground-based observatories through several atmospheric windows. Although these windows are poor compared to the optical and near infrared windows, they are usable at observatories where the atmosphere is particularly dry. This article is a discussion of the present status of submillimetre work but I shall not discuss observations of the 3 K background radiation or of the planets, as these have been reviewed recently^{1,2}.

Transmission of the Earth's Atmosphere

Figure 1 shows the transmission of the Earth's atmosphere in the infrared and submillimetre regions based on refs 3–5 and our own experience. The principal source of absorption in the far infrared is water vapour, and the figure is an approximate representation of the transmission under conditions of 1 mm of precipitable water vapour. It is clear that the atmosphere is opaque in the 100 μm region so that astronomical observations have to be carried out from aircraft flying at the top of the troposphere, or from balloons and rockets at yet higher altitudes. There are rather poor atmospheric windows in the 30 μm region, and again at 350 μm and longer wavelengths. These are usable for astronomical observations at sufficiently dry observatory sites. Several groups have begun to observe in these windows.

Under good conditions, the atmospheric transmission in the windows at 350 μm , 450 μm , and 650 μm is sufficiently stable to be represented by the exponential extinction law $\exp(-\alpha(\lambda) l \rho)$, where $\alpha(\lambda)$ is the intrinsic extinction coefficient, l the air mass in the line of sight, and ρ the precipitable water vapour. As it is notoriously difficult to estimate the atmospheric precipitable water vapour content, especially in night observations, I hesitate to quote absolute transmissions in these windows as a function of precipitable water vapour. The transmission at 350 μm is 30% for approximately 1 mm of precipitable water vapour in the line of sight (the uncertainty is in the calibration of the spectral hygrometer). Our measurements of the relative transmissions

$\alpha(350 \mu\text{m}) = (2.2 \pm 0.1) \alpha(1,000 \mu\text{m})$. From limited data from the few occasions when submillimetre observations, and 20 μm observations by the University of Hawaii group, were carried out simultaneously at Mauna Kea observatory, we estimate that $\alpha(350 \mu\text{m}) = (4 \pm 0.5) \alpha(20 \mu\text{m})$.

Galactic Sources

Direct observations of the emission of the coldest regions of our Galaxy must be made in the far infrared. Far infrared emission has been detected from HII regions and from regions of molecular emission at microwave frequencies. These observations are valuable for determining the total energy budget of these regions and the temperature and density of the interstellar dust in them. So far most observations have been in the 100 μm region from airborne platforms. Recently many of the same sources (as well as new sources) have also been observed at 350 μm and 1 mm. The telescope aperture in the ground-based observations is generally much larger than that available to the airborne work, so the observations at 350 μm and 1 mm have the advantage of much higher diffraction-limited spatial resolution. The sources are characterised by prodigious fluxes in the far infrared: for example, the 100 μm survey of 750 square degrees principally along the galactic plane carried out to a limiting sensitivity of $10^{-22} \text{ W m}^{-2} \text{ Hz}^{-1}$ yielded seventy-two sources. Of these, forty-six are clearly identified with HII regions (which in many cases contain radio molecular sources). Significantly, only one source discovered in the survey is possibly associated with a stellar object. Far infrared astronomy of galactic objects is thus distinctly the astronomy of extended objects. There is strong evidence that the emission of these objects is continuum emission since observations at 100 μm of a

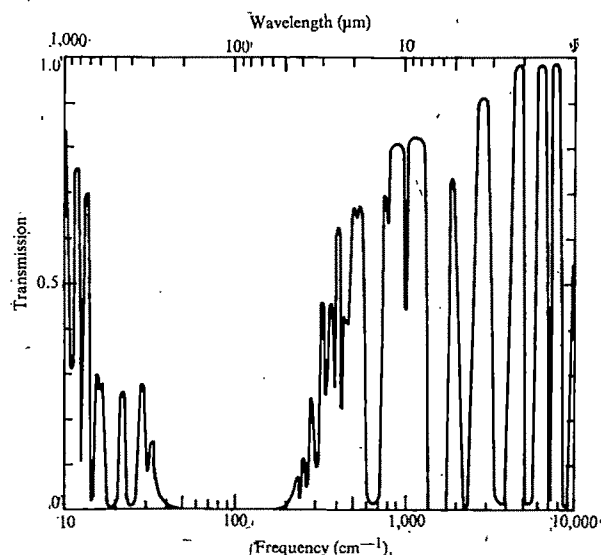


Fig. 1 Transmission of the Earth's atmosphere at infrared and submillimetre wavelengths. The transmission is intended to be roughly representative of conditions of 1 mm precipitable water

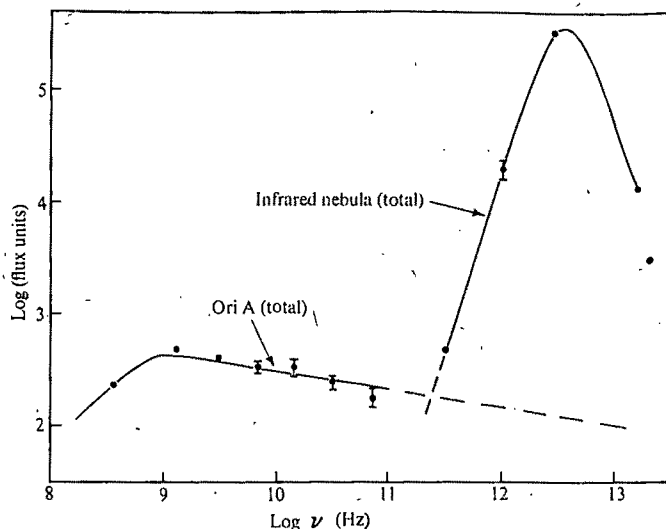


Fig. 2 The spectra of the total radio free-free continuum flux density of Ori A, and the total submillimetre flux density from the Kleinmann-Low infrared nebula. As discussed in the text, the positions of the strongest emission from Ori A and the infrared nebula are separated by about 1 arc min. The submillimetre data are discussed in the text, and the radio data are from refs 43 and 44.

given source (for example, the well studied sources in Orion and the galactic centre regions) by different observers with similar beamwidths but differing spectral bandpasses yield similar flux densities⁷⁻¹². As dust is present in HII regions, and as many of the far infrared sources are also molecular sources (the dust is implicated as the catalytic agent in molecule formation), the most reasonable assumption is that the far infrared emission from these sources is the thermal emission of the dust grains. As I shall discuss later, the 20 μm , 100 μm , 350 μm and 1 mm data from the Orion far infrared source fit a thermal emission model quite well.

The mechanism of the heating of the dust is still poorly understood. The two possibilities considered involve very different assumptions about the nature of the far infrared sources. In the first, the emission is presumed to originate in a dusty Stromgren sphere^{8,11,13}, so that the HII region, as delineated by its Lyman continuum, and the far infrared source should be spatially coincident. In this model the heating of the grains is due to Lyman α radiation of the gas and direct radiation from the exciting stars. Supporting this view, Harper and Low⁸ in their original observations of HII regions in a 40 to 750 μm pass band found a rough proportionality between the observed far infrared flux and the free-free continuum flux density at 2 cm. Similar correlations have been found by the other groups^{11,14} observing HII regions at 100 μm . But all observers find that the Lyman α energy available (as estimated from the excitation of the HII region) is less than the energy required to account for the far infrared flux by about an order of magnitude. Johnson¹⁵ has shown that the total stellar luminosity and the far infrared are about equal in a number of HII regions. In the HII region M42 (in Orion), however, the exciting stars are separated by at least 1 arc min from the far infrared source so that it is not clear that the far infrared luminosity can be attributed to the energy input of the observed stars.

The other point of view is that the far infrared emission is not from dust in the HII region itself, but rather from dust in the dense molecular clouds that are associated with it¹⁵ (a detailed model of the possible association of the molecular cloud in Orion with the rest of the HII region is given in ref. 46 by B. Zuckerman). In this view, the heating of the dust grains could be caused by stellar or proto-stellar objects embedded in the cloud¹⁶. Ground based observations have

and unpublished work of D. Y. Gezari, R. R. Joyce, G. Righini and M. Simon) and DR21 (Rieke *et al.*⁴⁷) peaks at the position of the strongest molecular spectral line emission rather than at the peak of the radio free-free continuum. In Orion this emission is at the position of the strong 20 μm extended source discovered by Kleinmann and Low¹⁸, and in DR21 at the position of the OH source. The 1 mm emission from these sources also peaks at the positions (ref. 48 and private communication from P. A. R. Ade and J. D. G. Rather). Similarly, Emerson *et al.*¹¹ found that in several instances the peak of 100 μm emission from HII regions is displaced from the radio continuum peak.

Further high resolution observations in the far infrared are required to find the relative importance of these two contributions to the far infrared emission of HII regions, and very likely both processes will turn out to be important. For example, in an HII region such as M17, which does not (as far as is known) contain a very dense molecular source, and in which the strong 10 μm emission is coincident with the strongest radio-free emission¹⁹, the far infrared emission may well arise entirely from dust grains heated by ultraviolet radiation. Orion appears to have both kinds of sources. The Ney-Allen source²⁰, which peaks in the near infrared (this source is approximately centred on the Trapezium stars which are believed to be the exciting stars for the M42 nebula), can be accounted for naturally by emission from ultraviolet-heated dust. The second type of source is the Kleinmann-Low/molecular source which, as we have seen, gives rise to the far infrared emission. Finally, there are far infrared sources associated with dark clouds⁷ from which no radio free-free emission is known.

The two far infrared sources studied in greatest detail are the Kleinmann-Low/molecular source in Orion, and the complex of sources near the galactic centre. Figure 2 shows the spectrum of the total flux density of the KL source; as the source is extended, the plotted points are those believed to include the bulk of the flux from the source. The 20 μm total flux density is from Low²¹, the 100 μm flux density is from Hoffmann, Frederick and Emery⁷ and was obtained with a beam of 6 arc min, the 350 μm spectral point was obtained by Gezari *et al.* (unpublished) with a beam of 3.5 arc min, and the 1 mm flux density is the total obtained by Ade and Rather (private communication) by mapping over an area of 4 arc min diameter. The 100 μm , 350 μm , and 1 mm points, of course, include both contributions from the Ney-Allen source and from the free-free continuum radio source. The former is quite negligible relative to the KL source at submillimetre wavelengths. The free-free contribution is certainly negligible at 100 μm and 350 μm , but it makes a significant contribution at 1 mm as indicated by the extrapolation of the radio-free emission in Fig. 2. Kleinmann and Low found that the observed flux density and size at 22 μm could be fitted by an optically thick thermal distribution ~ 70 K (ref. 18). The spectrum in Fig. 3 supports this interpretation. As the observed flux density decrease at wavelengths longer than 100 μm is steeper than the ν^2 dependence given by the Rayleigh-Jeans Law, the source must be optically thin with a frequency-dependent optical depth at these wavelengths. It may be shown (ref. 15 and unpublished work of Gezari *et al.*) from general considerations based on the Kramers-Kronig dispersion law that $\tau(\nu) \propto \nu^2$ in the long wavelength limit. Calculations of the optical depth of silicates²², based on measurements of the optical constants of silicates in the lunar soil²³, fit this low frequency behaviour well. Thus, in the low frequency limit, the flux density from an optically thin isothermal dust cloud may be expected to have a ν^4 dependence. (A temperature distribution within the cloud could make the frequency dependence less steep.) The submillimetre data in Fig. 2 at wavelengths longer than 100 μm fit this model well (when correction for the free-free contribution to the 1 mm flux density is made). The frequency-

the temperature of the source. Detailed analysis of this data shows (unpublished work of Gezari *et al.*) that the temperature is probably from 60 to 74 K, in agreement with the results of Kleinmann and Low, that the source is becoming optically thin at $100\ \mu\text{m}$ and that $\tau(100\ \mu\text{m})$ must be between 0.2 and 5. As the observations from which these conclusions are drawn represent fluxes from the entire source, the values of the parameters quoted here must be regarded as averages over the source. There is no difficulty in accounting for the high optical depths at submillimetre wavelengths. The molecular radio observations show that the molecular hydrogen density might exceed $10^7\ \text{cm}^{-3}$ in the core of the molecular source²⁴. Using typical values for the grain absorption efficiency for silicates, a normal gas-to-dust ratio, and grain mass density of $1\ \text{g cm}^{-3}$, one then naturally obtains values of $\tau(100\ \mu\text{m})$ of order 1 through the molecular cloud. Integrating the submillimetre spectrum in Fig. 2 and taking 500 pc for the distance to the Orion nebula, the total luminosity of the KL nebula/molecular source is $4.8 \times 10^{38}\ \text{erg s}^{-1}$. As noted by Hartmann¹⁶, this luminosity is several orders of magnitude greater than could be reasonably accounted for by the gravitational collapse of the cloud, and the most probable source of heating the cloud is the radiation of one or several early type stars.

A tentative general conclusion from this analysis of the radiation from the KL nebula/molecular source is that molecular sources known to be very dense (that is, sources in which transitions of molecules requiring high molecular hydrogen densities for collisional excitation are observed) may be expected to have high enough optical depths at submillimetre wavelengths to be strong submillimetre sources. This is indeed the case in W49, W51, DR21(OH), and Sgr B2 which have been detected from $100\ \mu\text{m}$ to 1 mm (refs 7, 8, 15 and 47, and private communications from Ade and Rafter and from M. W. Werner and P. M. Harvey).

The strongest far infrared source known, after the Sun and the Moon, is the complex region of the galactic centre. Its spatial extent, as revealed by the airborne $100\ \mu\text{m}$ observations, is $1^\circ \times 2^\circ$. Hoffmann, Frederick, and Emery²⁵ mapped this remarkable region at $100\ \mu\text{m}$ (Fig. 3) and found excellent agreement between the regions of far infrared emission and 2 cm radio emission, which is again free-free emission, except for the nonthermal source Sgr A. The peaks in their map also coincide with the known molecular clouds in this region. One of these, Sgr B2, is the richest source of molecular emission known²⁶, and has also been studied at $350\ \mu\text{m}$ (refs 14, 47 and unpublished work of Gezari *et al.*). The molecular source is quite large and probably has a dense core. The core is apparently smaller than 5 arc min and is probably about 1 arc min in size^{27,28} (at the distance of Sgr B2 this corresponds to ~ 3 pc).

The great spatial extent of this source makes comparison of different flux measurements (even at the same wavelengths) difficult for two reasons. First, the observed flux clearly depends very strongly on the beamwidth so the beam pattern must be known accurately in order to deduce the source brightness. Second, all the observations use some type of sky chopping scheme where the source signal is differenced against a position on the sky some distance away (usually small for technical reasons). This observing technique measures the derivative of the source brightness distribution. Clearly, chopping arrangements with large beam spacing (or, ideally, an absolute temperature reference as used in the rocket infrared observations¹³) are to be preferred. The present $350\ \mu\text{m}$ observations illustrate the difficulties of comparison of observations with different instrumentation. Observations of Sgr B2 with a 1 arc min beam and beam spacing of 4 arc min show a source of half power width ~ 3 arc min (N-S) $\times \sim 2$ arc min (E-W) and a peak flux density of about 8,000 flux units (Rieke *et al.*⁴⁷). On the other hand, observations of the same area with a 3.5 arc min beam

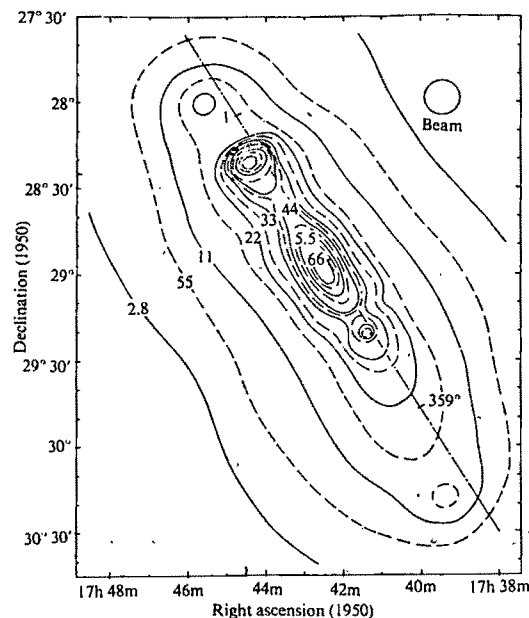


Fig. 3 Contour map of the galactic centre region at $100\ \mu\text{m}$ reproduced from ref. 25. The source Sgr B2 discussed in the text is within the northernmost of the three strong sources. (Reproduced with permission from *The Astrophysical Journal*, University of Chicago Press.)

$\sim 50,000$ f.u. and an extent 5 to 10 arc min E-W and about 10 arc min N-S (ref. 15 and unpublished work of Gezari *et al.*). These latter observations are in rough agreement with the structure in the $100\ \mu\text{m}$ map in Fig. 3. The two sets of $350\ \mu\text{m}$ observations are reconcilable and should be taken to be complementary. Thus the relatively small component is probably the dense core of the molecular source discussed already, and is seen superimposed on the more extended source.

Finally, it is interesting that the far infrared sources discussed so far have very little emission outside the $20\ \mu\text{m}$ to 1 mm band. At low frequencies, the approximately ν^4 flux density decrease makes detection difficult at radio wavelengths. For example, scaling the $350\ \mu\text{m}$ flux density of Orion to 3.5 mm suggests that the thermal emission from the dust in the molecular cloud should contribute only ~ 2 f.u. in a 3.5 arc min beam at 3.5 mm. Such a small contribution may be difficult to disentangle ambiguously from the very strong contribution due to the free-free emission. In a 3.5 mm survey of many far infrared sources, including Orion, Brown and Broderick²⁹ were unable to detect such an excess flux. It seems likely, however, that the upturn at 3.5 mm in the radio spectrum of the remarkable source Sgr B2 observed by Hobbs *et al.*³⁰ is from the tail of the far infrared emission. On the other hand, these sources are difficult to observe at wavelengths shorter than $20\ \mu\text{m}$ since their temperatures are so low. But submillimetre astronomy of galactic sources is still young, and the present results suggest that further observations will provide a valuable probe of the physical conditions in the cold components of the interstellar medium.

Solar Atmosphere

The radial temperature distribution of the solar atmosphere has a minimum between the photosphere and the corona in a region spanning nearly 500 km which is exceedingly difficult to study. Here I discuss the role of submillimetre observations in defining a model for the physical parameters in this region, their implications for the region's structure, and the potential contribution of these observa-

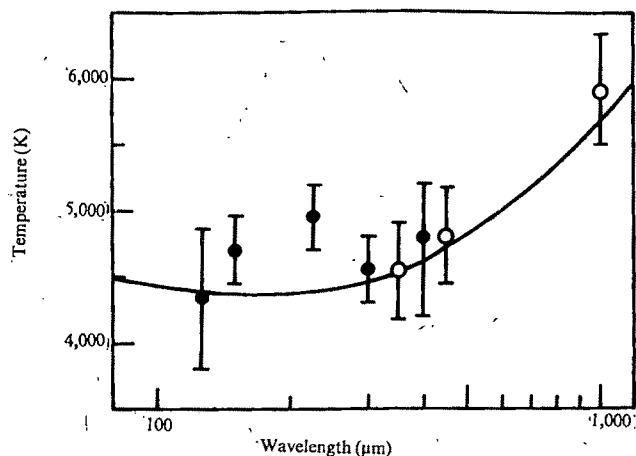


Fig. 4 The brightness temperature at the centre of the solar disk as a function of wavelength as given by the HSRA model³⁶. The data points are those published since the publication of the HSRA and are from ref. 6 (○) and ref. 37 (●).

The continuum radiation from the temperature minimum is assessable only in the rocket ultraviolet, or in the submillimetre region of the spectrum. The submillimetre continuum is perhaps more directly tractable since the source of opacity (free-free absorption due to the H^- ion) is well understood, and no strong emission features, unlike in the ultraviolet, are expected. Submillimetre observations of the solar brightness temperature as a function of wavelength at the centre of the disk may thus be inverted into the distribution of the temperature in the solar atmosphere as a function of optical depth. Submillimetre observations have already played an important role in this respect. Airborne observations in the 50 to 300 μm regions³¹⁻³³ and recent rocket observations³⁴ have indicated that the temperature minimum is 4,300 K rather than 4,600 K as had been previously inferred. This revision alleviates difficulties in understanding the 4,300 K temperature at the core of the Ca K line³⁵ and has been incorporated in the HSRA model of the atmosphere³⁶. Fig. 4 shows the temperature profile as a function of wavelength given by the HSRA model at submillimetre wavelengths. As the HSRA was adjusted to fit the best data available at the time, I show in Fig. 4 only measurements^{6,37} obtained subsequent to the publication of the HSRA. (Comparison of the HSRA with the data available at the time of its publication is in Fig. 2 of ref. 36.) The agreement of recent data with the HSRA is quite satisfactory. The strong upturn at $\lambda > 500 \mu\text{m}$ is dictated by the high brightness temperatures measured at 1 mm and longer wavelengths. There are no observations available of the brightness temperature between 500 μm and 1 mm, representing a factor of four in the optical depth, so data are needed to delineate the temperature distribution in this region.

Further information on the temperature distribution and structure of this region may be derived from the brightness temperature variation across the disk. For example, if the solar atmosphere is homogenous and spherically symmetric, the brightness temperature distribution should be entirely determined by the variation of central brightness temperature with wavelength, and the parameter $\lambda^2/\sqrt{1-r^2}$, where r is the fractional distance to the limb from the centre of the disk. In the HSRA model the temperature minimum occurs at about 200 μm . Limb darkening should be observed at longer wavelengths; the HSRA model predicts $\sim 5\%$ limb brightening at 350 μm at $r=0.8$. Our scanning observations at 350 μm appear to rule out this degree of limb brightening. Limb darkening at 1 mm has been reported^{38,39}, but recent observations at 1 mm, in which a detailed analysis of the beam pattern was made, seem to be consistent with no limb

P. E. Clegg). Departures from the limb brightening predicted by a homogenous model with the HSRA temperature profile may be interpreted in terms of either a revision of the temperature gradient in the HSRA, or a dropping of the homogeneity assumption. In view of the good agreement of the model with the brightness temperature measurements at the centre of the disk, and the well-known inhomogeneity of the solar atmosphere both above and below the region of the minimum, it is likely that here too the homogeneity assumption will have to be relaxed.

High resolution mapping observations at these wavelengths may also be expected to improve understanding of the electron density and temperature of active regions. Ade *et al.*⁴⁰ have mapped one active region at effective wavelengths 400 μm , 800 μm , and 1,200 μm , and found that the brightness temperature increased from 200 K at 400 μm to 350 K at 1,200 μm . These submillimetre observations may indicate the existence of a dense core of the active region that is nearly optically thick at these wavelengths. Further observations of active regions, and detailed comparison with radio observations, are clearly required.

Future Prospects

Submillimetre observations of extragalactic objects are still sparse, although the observations so far show it to be an area of great promise. NGC1275, M82 and 3C273 have been detected at 1 mm (unpublished work of Ade and Rather), NGC253 (Rieke *et al.*⁴¹) and possibly M82 (ref. 41) at 350 μm (although the flux calibration for M82 is almost certainly in error), and M82 and NGC253 at 100 μm (ref. 42). The millimetre wavelength radiation of sources such as 3C273 and NGC1275 is known to be non-thermal, and at least part of the flux is time-varying and believed to originate in rapidly-evolving small components. Observations of variability at submillimetre wavelengths would place severe restrictions on the models of these components. It is premature to speculate on the nature of the submillimetre radiation of objects such as NGC253 (which is the strongest extragalactic source at 10 μm) and M82, but the radiation may well be thermal.

Technically there are several promising areas. Fainter objects will become observable through the use of larger apertures and stabilised observing platforms in the airborne work, and the development of more sensitive detectors for both the ground-based work and airborne work (because in both the limiting noise at present is detector noise). This discussion of submillimetre astronomy is based on data obtained by broad-band photometry or very coarse resolution Michelson interferometry. There is a great incentive to develop submillimetre spectral line systems to observe fine structure lines, recombination lines, and molecular lines that are accessible in this region of the spectrum and to use them as astrophysical probes. Several active developmental programmes are under way, and it is probably not too optimistic to believe that in a few years the time will be right for a similar preliminary review of submillimetre line astronomy.

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Conditions Limiting Multiplication of Fibroblastic and Epithelial Cells in Dense Cultures

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The multiplication of epithelial cells in plastic dishes is limited by the amount of plastic surface available per cell, that of fibroblastic cells by the availability of medium factors. Contacts between cells do not appear to limit the multiplication of either cell type. The multiplication of fibroblastic cells is even favoured by shorter intercellular distances, suggesting a distance-dependent helper effect between cells.

CULTURES of untransformed cells growing on a glass or plastic surface display the phenomenon of "density-dependent growth inhibition": under standard conditions of

cultivation cell multiplication stops when a certain cell density, characteristic for each cell type, is reached. If a strip of cells is removed from a stationary culture, cells migrating from the borders into the denuded area (the wound) are activated to multiply, although the medium remains unchanged¹. It has been shown that the activation occurs when the cells leave the dense layer². The differential ability of the cells in the wound to initiate DNA synthesis in comparison to those in the layer has been defined as topoinhibition³. Although topoinhibition is a useful parameter for characterising cell lines, especially in relation to transformation, its mechanism is undefined. The basic dilemma is whether the multiplication of cells in the layer is inhibited by the intimate contacts between cells ("contact inhibition of growth") or by a lower ability to utilise components of the medium, especially serum⁴. The reason for the uncertainty is that most experimental procedures affect many variables at once.

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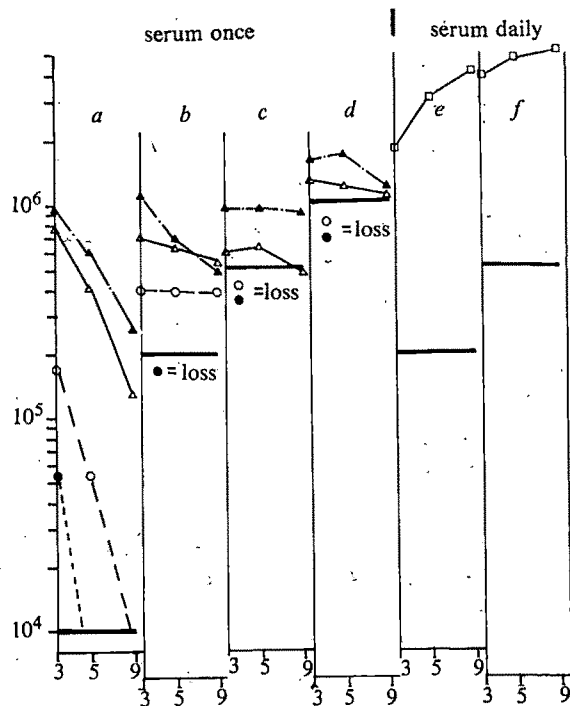


Fig. 1 Final number of Balb/c 3T3 cells in cultures of different size. Approximate dish diameters in centimetres are shown on the abscissa. *a* to *d*: Single supply of medium with the following concentration of calf serum: $\blacktriangle$, 20%; $\triangle$, 10%; $\circ$, 5%; $\bullet$, 2%. *e*, *f*: Daily change of medium with 10% serum. The number of cells in the inoculum of each set is indicated by the heavy horizontal line. The lines connecting cell numbers for different size dishes and the same concentration of serum terminate at the inoculum level when the next point is below that level, that is, there was loss of cells. Loss of cells at all three dish sizes for a certain concentration of serum is indicated by placing the symbol for that serum concentration below the inoculum line.

Varying Dish Size

The experiments we are now reporting are aimed at clarifying the role of cell-to-cell contacts under conditions in which the availability of medium is constant. To this end we have studied the effect of a single variable, the amount of dish surface available to each cell, on the number of cells present per dish at saturation, using the following scheme. Parallel cultures were prepared, each with the same number of identical trypsinised cells and in the same volume (6 ml) of medium (reinforced Eagle's containing calf serum at the indicated proportions), but in dishes (plastic, Nunc) of different sizes: 30, 50 and 90 mm in diameter. Hence the dish size was the principal variable. In the 30 mm dishes the depth of medium was about 7 mm, about 1 mm in the 90 mm dishes. The plastic area available to each cell in the 30 mm dishes was, on the average, about one-eighth that in the 90 mm dishes. The cultures were maintained in a CO_2 -flushed, high humidity incubator and were allowed to grow without medium changes until growth stopped, as shown by the absence of mitoses. The validity of this criterion was confirmed in some cases by growth curves. Usually, growth stopped somewhat sooner in the 30 mm dishes: 4 to 7 d, depending on initial cell density, compared with 5 to 10 d in the 90 mm dishes. After growth stopped, the cells were detached with trypsin and counted in a Coulter counter. Several cell lines were used: Balb/c 3T3 (ref. 6) and BHK 21 (Cl 13) (ref. 7), fibroblastic; CV-1 (ref. 8), and BSC-1 (ref. 9), epithelial; and SV3T3 (ref. 10) and Py BHK (produced in this laboratory), transformed. In different experiments the inoculum varied between 10^4 and 10^6 cells per dish, and the serum concentration in the medium between 2% and 20%.

In this protocol the main variable is the distance between cells, which in turn affects the extent of contact between them, their ability to move and to stretch. Two other variables, the depth of medium and possibly the nature of the plastic employed in the manufacture of dishes of different sizes, seem to be of little importance on the basis of internal controls, as indicated below.

The experiment has three possible outcomes. If the area of the plastic surface available to a cell limits cell multiplication, the final number of cells in a dish should be proportional to the surface of the dish. If, on the other hand, growth is limited by medium components, the final cell density should be equal on all size dishes. Finally, if there is a distance-dependent helper effect between cells (for instance, if growth is helped by cell-to-cell contacts or by labile substances produced by the cells), the number of cells should be inversely related to the dish surface.

The results with Balb/c 3T3 cells, which are characterised by a high topoinhibition and high serum requirement⁶, are given in Fig. 1*a* to *d*. When the cell inoculum and the serum concentration were high, the dependence of final cell number on dish size was that expected from limitation by medium. When the cell inoculum and the serum concentration were small, the relation conformed to that expected from a distance-dependent helper effect.

The latter result might also have been produced by loss of medium components to the walls of the dish, which would be more pronounced in the larger dishes. This possibility was tested by incubating the medium in the dishes for 3 d and then adding cells to it (5×10^5 per dish). The final number of cells per dish was about half that of similar cultures whose medium had not been preincubated, irrespective of dish size. Thus there is no evidence for loss of medium to the plastic, but only for partial inactivation. Conceivably, the effect may be due to loss to the walls of some growth factor present in the cell inoculum; but this possibility was not tested. Under no circumstance was there evidence that the available dish surface was limiting the growth of these cells.

The distance-dependent helper effect affects the growth rate of the cells, which is slower in the larger dishes (since they produce fewer cells in a longer time). The lower final cell number on the larger dishes may be due to greater inactivation of medium components, since a longer time is required to reach saturation.

We tested whether a dish surface requirement for Balb/c 3T3 cells became demonstrable when the availability of medium was increased by growing cultures with daily changes of 10% serum medium. As shown in Fig. 1*e* and *f*, these cells reached a resting stage with a larger number of cells per culture; but although the relation of final cell number to dish size showed some dependence on available surface, limitation of medium was still the most important factor stopping growth.

These experiments were repeated several times with similar results: similar results were also obtained with BHK cells.

Some other results of these experiments should be noted. In the first place, cultures with the same serum concentration and similar initial density of inoculum cells (and therefore similar helper effect) tended to yield similar (within a factor of two) final cell numbers irrespective of dish size (compare for instance points *d*9 with *b*3 and *b*9 with *a*3 in Fig. 1). This shows that the depth of the medium and the nature of the plastic have a minor importance for the final number of the cells. In the second place, when the ratio of cells to serum in the inoculum was small the final cell number was lower than the inoculum, indicating loss of cells. This result suggests that cell survival depends on a stoichiometric relationship between serum and cells. A stoichiometric relationship also holds between amount of serum and number of new cells produced, 0.06 ml serum corresponding to about 5×10^6 Balb/c 3T3 cells. This relationship

shows that the access of medium components to the cells is not affected by the degree of cell overlaps.

The epithelial cells of the BSC-1 and CV-1 lines, which have a high topoinhibition but a low serum requirement⁴, gave different results (Fig. 2). In all cases growth was limited primarily by the restriction of dish surface, especially when 10% serum was used. There was also, however, some medium limitation or helper effect because the cell numbers on 90 mm dishes were at most five times those on 30 mm dishes, although the dish surfaces differed by a factor of eight.

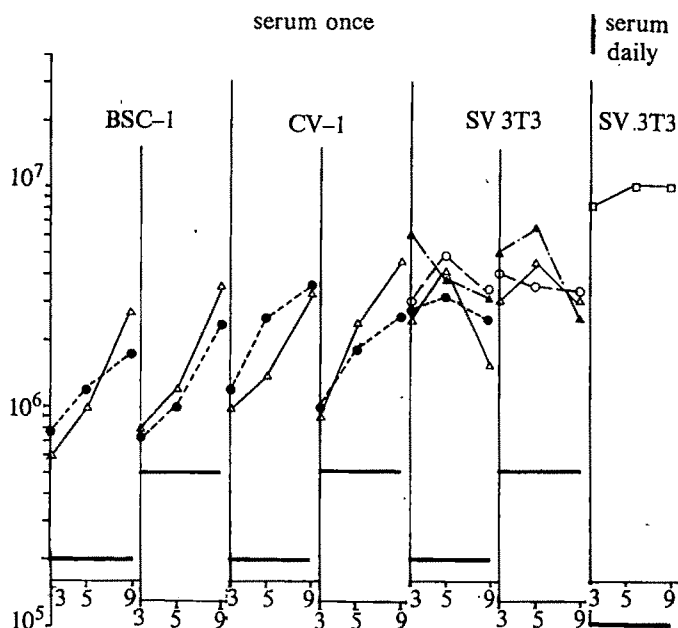


Fig. 2 Same as for Fig. 1, except for the last set, which had daily change of medium with 10% calf serum, there was a single supply of medium in all cases. For symbols referring to serum concentration see Fig. 1.

For transformed SV3T3 cells which have very low topoinhibition and serum requirements⁴ (Fig. 2) there was little effect of either the amount of serum or dish size in the range used. A similar result was obtained with Py BHK cells. With SV3T3 cells, changing the medium daily increased the final cell number to a constant value irrespective of dish size. Hence there is no evidence that these cells have a dish surface requirement even when medium is plentiful. It should be noted, however, that transformed cells did not attain a stationary stage: growth was stopped by the spontaneous detachment of the cells from the plastic.

Growing and Stationary Cultures

The result that under standard culture conditions multiplication of Balb/c 3T3 or BHK cells is not stopped by restriction of available dish surface shows that their growth is not limited by contacts between cells or by their inability to move or to stretch. Before this conclusion was used to explain the results of wound experiments, we examined the possible role of a difference in the two experiments. The present experiments study the effects of cell crowding on growing cultures, whereas the wound experiments employ already crowded and stationary cultures. The role of this difference was tested by varying the experimental procedure: Balb/c 3T3 cells were seeded in exhausted medium (origin-

resting cultures of the same cell type and diluted with the addition of fresh medium without serum (half the volume). The cells did not grow but formed stationary cultures. Then serum was added to a concentration of 10% to start growth. The results obtained were similar to those obtained by the standard procedure.

Fibroblastic and Epithelial Cells

These experiments suggest that cell multiplication is limited by different mechanisms in fibroblastic and epithelial cell cultures and, accordingly, that the significance of the wound experiment and of topoinhibition are also different.

With fibroblastic cells, a restriction of the available surface to which they adhere only begins to limit growth at extraordinarily high cell densities. Under usual culture conditions their multiplication is stopped by the exhaustion of medium components, especially serum. Therefore, activation of fibroblastic cells that migrate from a dense layer into a wound is likely to be caused by their ability to utilise the medium more efficiently. Indeed, Stoker¹¹ has shown that there are important differences in the state of cells in a layer and of isolated cells as are found in a wound, in that isolated cells have better access to the medium. Probably the limitations in the layer are not affected by its density within a broad range.

In contrast, with epithelial cells a dish surface restriction is the predominant factor stopping growth; hence the increased availability of dish surface to the marginal cells after wounding may contribute to activate their growth. However, even for these cells it is unlikely that the dish surface requirement has to do with an inhibitory effect of contacts between cells. In fact, the epithelial cultures become resting long after the cells start touching each other; and when the cultures are wounded the cells at the edge of the wound do not become free from each other (except, perhaps, transiently during wounding) but migrate as a sheet, at the same time expanding their surface¹².

Topoinhibition seems to result from different mechanisms in fibroblastic and epithelial cells; lower utilisation of medium components by cells in a layer in the former case, and a dish surface requirement (also perhaps with a decreased medium utilisation in the layer) in the latter case. The dish surface requirement may be an attribute of cells that must form a monolayer, as many epithelial cells do in nature in relation to their basal membrane. Fibroblastic cells need not form a monolayer either in nature or in cultures.

On the basis of the foregoing, we believe that there is no experimental support for the concept that "contact inhibition of growth" is responsible for cessation of growth in dense cultures.

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Role of Diffusion Boundary Layer in Contact Inhibition of Growth

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Use of a miniature pump to produce a local increase in velocity of medium across the surface of confluent 3T3 cells stimulates growth which is limited to the region of high velocity. This indicates that growth is limited by a diffusion boundary layer close to the cell surface. The events at the edge of wounded cell layers (topoinhibition) can be explained by local variation in the fluid microenvironment rather than by alterations in contact between cells.

CONTACT inhibition of growth of cultured fibroblasts like contact inhibition of movement¹ has attracted much interest but the role of contact is still uncertain, and for this reason the alternative names density-dependent inhibition² and topoinhibition³ have been proposed. It is now acknowledged that the supply of medium⁴ and particularly serum⁵⁻⁷ plays an important part in this phenomenon. Nevertheless, it has been difficult on this basis alone to explain the very short-range topographical effects seen in wounded cultures, which have remained the strongest evidence that contact between adjacent cells plays a role in inhibition of growth in confluent cell layers.

When a strip of 3T3 cells is mechanically removed from a confluent non-growing monolayer, growth begins in those cells which migrate from the edge of the confluent sheet into the denuded area⁸, and in individual cells this can be correlated with loss of contact with neighbours⁹. Since the non-growing cells still in the confluent sheet and the growing cells in the wound are in the same medium only a few micrometers apart, it has seemed likely that the difference in growth is due to changes in the intimate relationship between cells, probably involving contact.

There is, however, an alternative explanation^{9,10}. This would suppose that the emigrating cells at the wound edge travel through and respond to a concentration gradient in the surrounding medium, affecting the availability of some substance critical for growth. At first sight it might appear that convective movement in the fluid should be sufficient to prevent the development of such a very localised gradient, but fluid movement is known to be reduced in the layer very close to the cell surface. A sufficient increase in the velocity of the fluid medium over a cell sheet might, however, perturb a local concentration gradient and alter the growth of the cells.

Riddle's Pump

For this purpose I have used a small pump developed from an agglutination chamber designed by Riddle¹¹ which

introduces a recirculating movement into the existing medium in the dish, in a narrow stream, 0.5 to 1 mm wide at velocities of up to about 100 mm s⁻¹. The pump (Fig. 1) consists of a glass capillary tube about 3 cm long and of 2 mm bore, narrowing to about 1 mm at the tip, which is lowered into the medium.

The other end of the tube is inserted directly or by a flexible connector tube into the opening in a hearing aid earpiece (Medresco OL575, Cosmocord Ltd, Waltham Cross, U.K.). The latter is attached to a variable transformer with an output of 2-3 V a.c. at 50 Hz. This causes oscillation in the medium in the capillary tube which is translated at the tip into a unidirectional outward flow. The jet of medium produced is a narrow stream which fans out about 5 mm from the tip of the capillary tube and then circulates slowly as shown in Fig. 1. It has not been possible to measure the velocity accurately with the current used, but it is more than 10 mm s⁻¹ in the centre of the stream with a theoretical maximum of 100 mm s⁻¹ calculated from the oscillatory excursion in the capillary tube. Close to the surface of the cell layer this is reduced to 2-4 mm s⁻¹. Away from the main stream, in the recirculation region, the velocity is reduced to 1-4 mm s⁻¹, and close to the cell layer in this region it is too slow to measure.

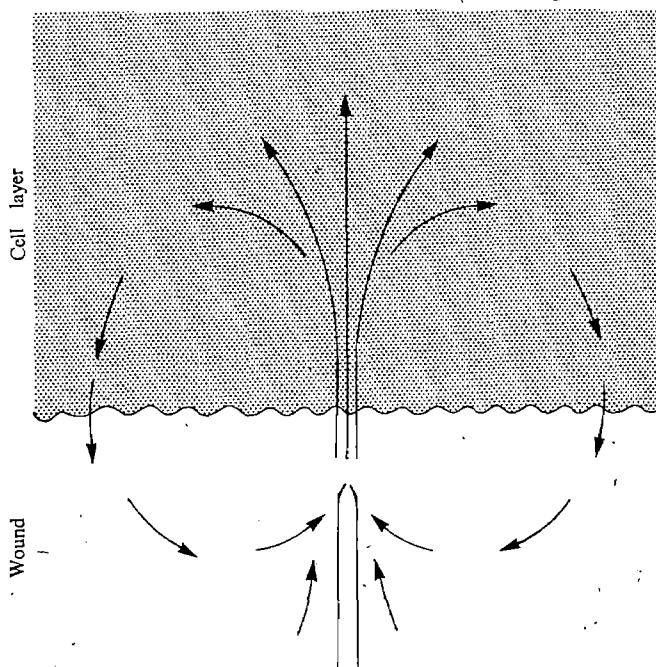


Fig. 1 Pattern of medium recirculation produced by pump across edge of cell sheet. Relative velocity indicated by length of arrows.

Cultures of Balb 3T3 cells were grown to confluence in Dulbecco's modification of Eagle's medium with 10% foetal calf serum, and left without medium change for 4-7 d before use. The stationary sheets were wounded with a razor¹² and in most experiments fresh medium was added with 5% serum which is sufficient to stimulate growth in about 10% of cells in a confluent layer. The pump was directed across the edge of the wound towards the cell sheet with the tip of the denuded area about 2 mm from the edge of the cell layer and was allowed to run continuously while cultures were incubated in containers flushed with 10% CO₂. Controls were set up under identical conditions but with no pump.

Effect of Increased Velocity of Medium

When the cultures were examined after 26 h the number of mitoses and total cell numbers per unit area were seen to be increased in a small region of the cell sheet exposed to the fastest stream from the pump (Figs 2 and 3). A few millimetres from the main stream, even in the recirculating region the numbers of cells and mitoses were similar to those found in the rest of the dish and in the control unpumped culture. The mitotic index, which allows for the variation in cell numbers, was highest in the centre of the stream, 2.7% (19/700) compared to 0.5% (5/950) elsewhere in the dish.

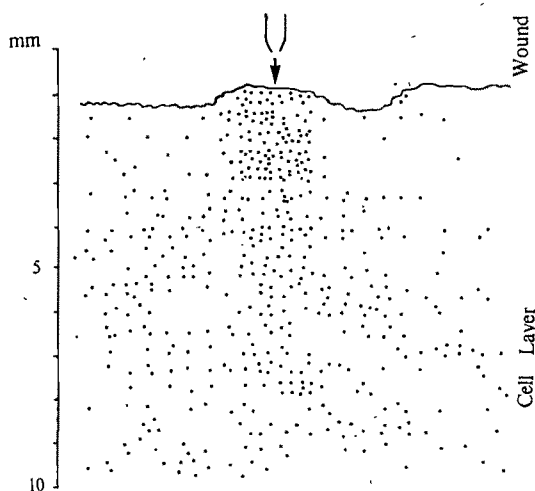


Fig. 2 Effect of local change in velocity of medium on distribution of mitoses. A strip of cells from a confluent stationary culture of 3T3 cells was removed with a razor, fresh medium with 5% calf serum was added, and the cultures incubated with the pump operating for 26 h, directed across the edge of the sheet. Each dot represents a mitosis at the distance shown from the pump.

After 22 h exposure to ³H-thymidine and subsequent autoradiography the distribution of labelled nuclei in the confluent sheet was similar to that shown for mitoses in Fig. 2. 76% of cells were labelled in the region of the jet compared to 10% elsewhere (at least 200 counted). In contrast 81% of cells emigrating into the wound were labelled irrespective of relationship to the jet.

Since cell density was increased and mitotic cells were not removed by the jet it seemed unlikely that the stimulation of growth was due to local reduction in cell density and contact caused by detachment of cells. This was confirmed by time lapse cinematography of the area in the stream, which showed no loss of cells. The film also showed that there was no displacement or distortion of cells in the direction of the medium flow. A temporary increase in local cell movement compared to unpumped cultures was seen which lasted up to 16 h. Since the movement stopped between 16 and 22 h, it was not due to a direct physical effect of the fluid movement on the cells.

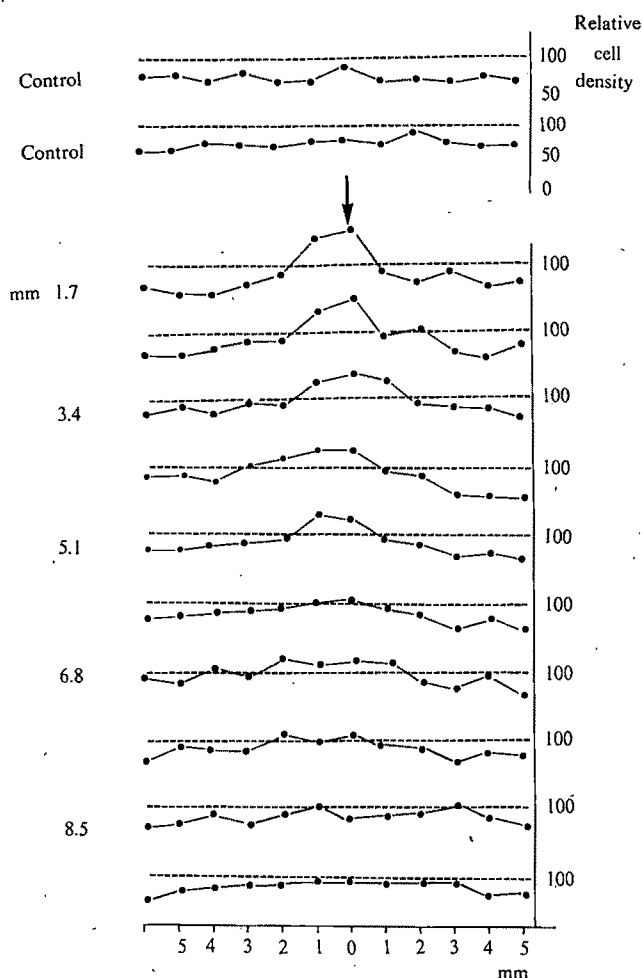


Fig. 3 Effect of local change in velocity of medium on cell numbers. Same culture as in Fig. 2. Cell numbers per unit area (0.15 square mm) are shown across the cell sheet parallel to the wound edge and at distances shown from the pump. Controls are (1) from the opposite side of the same layer (behind the pump) and (2) from a parallel but unpumped culture.

to be due to a direct physical effect of the fluid movement on the cells. It therefore seems likely that the stimulation of cell growth and movement with increase in velocity of the medium is due to concentration changes in the fluid micro-environment itself.

The Diffusion Boundary Layer

The behaviour of molecules in fluid close to a solid reactive surface has been extensively studied by physical chemists. Since the convective movement of most fluids approaches zero near a solid surface over which flow occurs, the transfer of molecules to and from the surface is largely limited to the relatively slow process of diffusion. This results in a diffusion boundary layer^{13,14} which can act as a barrier close to the reactive surface. If, for example, a cell rapidly removes a molecule essential for growth from the medium, the concentration near the cell surface will fall to a level determined by the uptake rate and the rate of replenishment by diffusion from the bulk of the medium. The supply of such a molecule may become limiting and the process (growth) then becomes diffusion controlled. The restriction can be relaxed by raising the concentration of the substance in the bulk medium, or alternatively by reducing the diffusion boundary layer. For a particular fluid the diffusion boundary layer is characteristic of each type of molecule and it is usually defined as the region with a concentration less than 90% of that in the bulk of the fluid¹³. Apart from the diffu-

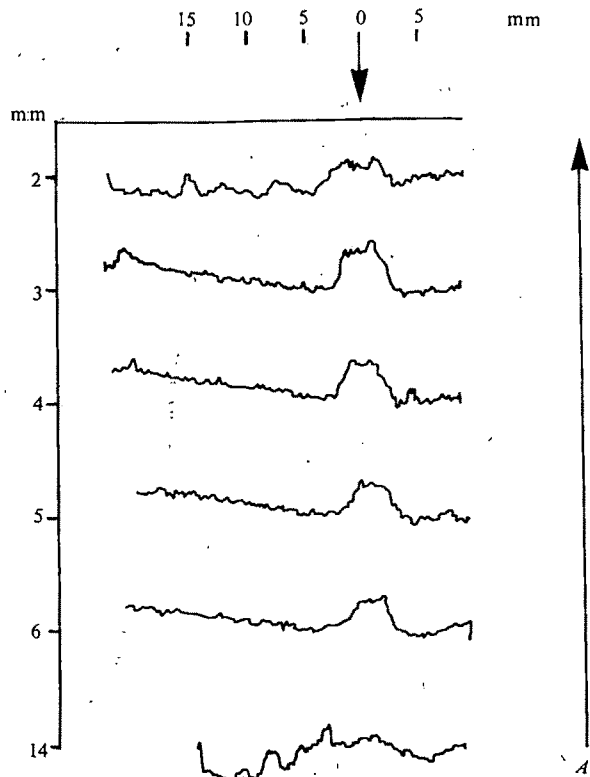


Fig. 4 Effect of local change of medium velocity on uptake of stain. A confluent layer of 3T3 cells was fixed and exposed to Giemsa stain (0.03%) with the pump operating. After 3 min, uptake of stain was measured by microdensitometer tracings at right angles to the fluid flow and at distances shown from the pump.

sion coefficient and the net loss to the reactive surface, which cannot be varied, the diffusion boundary layer is inversely proportional to the square root of the velocity of the medium flowing over the surface. The velocity can be increased and, as shown here, this does affect cell growth.

Effect of Velocity on Staining

The existence of a diffusion boundary layer, even over a fixed cell layer, may be demonstrated by the effect of velocity on uptake of a stain such as Giemsa stain. Staining of a confluent sheet of 3T3 cells may barely be detected after 3 min exposure to dilute Giemsa stain (0.03%). Use of the pump, however, to produce a local increase in fluid velocity over the sheet causes uptake of stain limited to the region of high velocity. Figure 4 shows microdensitometer tracings across a cell sheet at right angles to the fluid flow and at varying distances from the jet (see Fig. 3). It shows the increased absorbance due to higher stain uptake limited to the narrow band exposed to the stream of medium. By coincidence this corresponds topographically and therefore in velocity to the region of growth stimulation produced by the pump in living cell sheets. It does not follow, however, that a molecule limiting for growth is of a similar size to the methylene blue eosin in Giemsa, since the uptake rate may be different.

Growth in Wounded Cell Sheets

This investigation was carried out to find out if concentration changes in the medium over a wound could account for growth of cells migrating over a very short distance from the edge (of the order of one cell diameter). Assuming negligible uptake of a critical substance by the supporting plastic, there will be no diffusion boundary layer and no reduction in concentration of medium constituents over the denuded area

up to the edge of the cell sheet (or a single cell). At the wound edge, however, diffusion can occur laterally as well as vertically, so the boundary does not start abruptly. It increases in proportion to the square root of the distance from the edge of the sheet. This has been studied by chemists in the dye industry¹⁵, and even in fixed 3T3 cells uptake of Giemsa stain may be increased at the edge of a cell sheet compared to the rest of the sheet. It means that the concentration of a critical substance at the surface will be higher near the edge of a wound and then fall rapidly over the undisturbed layer as the diffusion barrier increases.

Since the critical substances themselves and many of the parameters are unknown, the shape of the resulting concentration gradient over the edge cannot be determined. If, however, the diffusion boundary layer becomes maximal over a distance of one or more cell diameters it will not be fully developed over isolated migrating cells or the single row of cells lining the edge, and the concentration of a limiting substance over such cells will not fall to the same level as that over the continuous sheet. Consequently, with limiting nutritional conditions, the growth of confluent cells would be restricted, while isolated cells which had migrated a short distance into the denuded area would be able to grow (Fig. 5a). A sufficient increase in the velocity of the medium would reduce the boundary layer and increase the concentration over the sheet (Fig. 5b).

It should be noted that an increase in velocity in any direction, not necessarily over a wound edge, will reduce the diffusion boundary layer. This has been confirmed by placing the pump over the cell sheet where it still stimulates

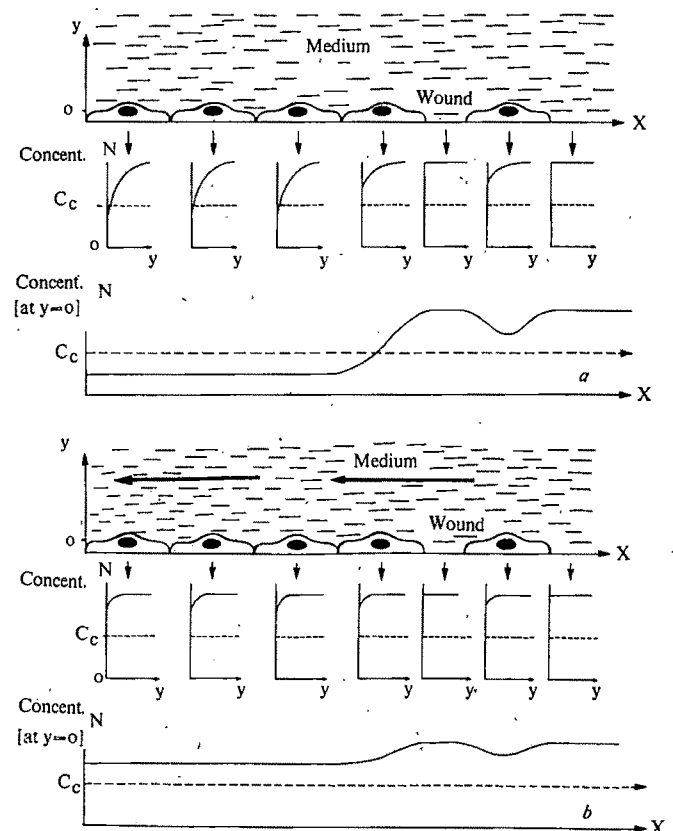


Fig. 5 a, Diagram showing changes in concentration of a hypothetical limiting nutrient across edge of a wound. Top part shows section of cell layer across wound with migrating cell on right, in stationary medium (convection only). Middle part shows concentration distribution vertical to cell sheet (y axis) over different regions. Lower part shows concentration distribution at the cell surface horizontally across the wound edge (x axis). C_c —concentration of hypothetical substance limiting growth of cells migrating over wound edge.

growth. When the medium flows towards the sheet from a denuded region without uptake of critical nutrients, however, the effect of the increased velocity is enhanced.

This paper emphasises the role of the diffusion boundary layer in limiting the uptake of critical nutrients or growth factors from the medium. The barrier could, however, operate in the opposite way, by preventing the escape of inhibitory molecules released by the cells. On present evidence the two mechanisms cannot be distinguished.

The original suggestion that a diffusion barrier could account for many of the effects of cell density was based on experiments with opposed cell layers made by Rubin and Rein¹⁰. My data support this view and show that concentration changes in the microenvironment could account for the highly localised growth of 3T3 cells at the edge of wounds and presumably also at the circumferences of colonies¹⁶. On this basis the reduction in density-dependent inhibition of growth, or topoinhibition, by virus transformation can be explained by a lowering of nutritional requirements. Even in those variants which show a lowered requirement for serum growth factor while remaining sensitive to topoinhibition¹⁷, another essential nutrient may be limiting.

It may be concluded that topoinhibition, as manifest at wound edges in 3T3 cells, is no longer evidence that contact between cells regulates their growth. The accompanying paper¹⁸ reaches the same conclusion on different grounds.

I am grateful to Dr P. Riddle for help with the pump and for time-lapse cinematography, to Mr Denis Piggott for technical assistance, and to Dr N. Maroudas for discussion.

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LETTERS TO NATURE

PHYSICAL SCIENCES

A Double Quasistellar Object

BECAUSE QSOs are rare^{1,2} the discovery of close pairs with discordant redshifts is improbable if they are randomly distributed on the plane of the sky. But Stockton³ has reported that Ton155 and Ton156 form a pair of 17 mag QSOs, with a separation of approximately 35 arc s. For QSOs randomly distributed on the plane of the sky he gives the probability for an accidental occurrence of this close pair as 6×10^{-8} .

Visually, 1548+115=4C11.50 (ref. 4) is another close pair of blue stellar objects. The brighter object (1548+115a) is approximately 17 mag, and is followed 4.8 arc s east and 0.4 arc s south by the 19 mag object 1548+115b. The pair was first noted by Hazard and Jauncey (see ref. 5) in a programme of 4C identifications, and has also been noted by Murdoch and Hazard (unpublished) in a programme of identifications based on Molonglo radio positions. It had been found earlier⁴ that 1548+115b was a QSO although its redshift had not been determined nor had the nature of 1548+115a been established. We report here that 1548+115a is also a QSO and give additional spectral information for both objects. In particular we note the very different redshifts of the objects; $z=0.4359$ for 1548+115a and $z=1.901$ for 1548+115b. The radio source is a 3C273 type double (Ekers and Fanaroff, private communication) with one component coincident with 1548+115a. There is a faint red wisp of otherwise unknown characteristics visible on the National Geographic Mount

On the nights of August 1, 3–6, and 24–25, 1973 (UT), 1548+115a,b were observed optically with the Cassegrain scanner⁶ of the 120-inch (305-cm) telescope. At that time of year 1548+115 can only be observed early in the evening in the western sky. The astronomical seeing was generally good during the earlier observing period and small (~ 2 arc s) spectrograph entrance apertures were used to reduce the background illumination from the lights of nearby cities. On the nights of August 24–25 the conditions were much poorer and only 1548+115a was observed. The use of small apertures, especially in the presence of substantial atmospheric dispersion, prevented us from obtaining an accurate continuum flux calibration. For this reason we are uncertain of the spectral index of the continuum although the magnitude estimates obtained in August ($m_v=16.8$ and 18.8) are in good agreement with those obtained earlier⁴. Our best estimate for the spectral index of 1548+115a is $\alpha=0.8 \pm 0.5$ and for 1548+115b $\alpha=0.6 \pm 0.4$ where α is the index in the equation $f_\nu \sim \nu^{-\alpha}$. Because the objects are so close together scattered light is a potential problem, but measurements of the scattered light from a bright star set 5 arc s off the slit showed no significant effects.

Both objects show rich emission line spectra. The observed lines, their identifications, and equivalent widths are listed in Table 1. The adopted redshift for 1548+115a is $z=0.4359$ and for 1548+115b we adopt $z=1.901$. If both objects were at the cosmological distance corresponding to $z=0.4359$ their separation would be about 40 kpc ($H_0=50 \text{ km s}^{-1} \text{ Mpc}^{-1}$, $q_0=1/2$). Figure 1 shows the observed spectra of the two objects. They seem to be normal for QSOs. Also the objects seemed stellar in the television guiding monitor of the 120-inch

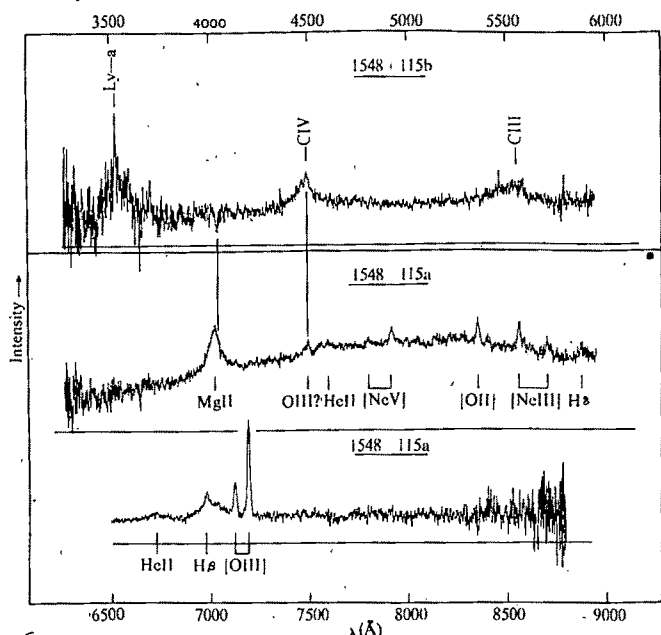


Fig. 1 Spectra of 1548+115a,b. Evidence of poor subtraction of the strong Hg night sky lines at $\lambda\lambda 3650, 4047$ may be seen in the spectra. But a close inspection of our data shows that the strong absorption feature seen at $\lambda 4038$ in the spectrum of 1548+115b is not caused by incorrect subtraction of Hg $\lambda 4047$. The two vertical lines show the correspondence between the $\lambda 4038$ and $\lambda 4495$ features in the spectra of 1548+115a,b.

would be classified as a normal QSO. In addition to the close proximity of the two objects to each other in the plane of the sky and the possible alignment of the optical and radio sources, there are several coincidences in the spectra of the two objects.

First, there is a strong absorption feature at $\lambda 4038$ in the spectrum of 1548+115b that lies slightly to the red of the redshifted Mg II $\lambda 2800$ emission peak in the spectrum of 1548+115a. The spectral data are not of high enough quality to decide conclusively if the feature is due to Mg^+ or to some other ion, such as C^{3+} . An accurate determination of the profile of the absorption line is hindered by the presence of a strong night sky line, Hg $\lambda 4047$, in the red wing of the feature. But we were able to use the night sky line to determine the instrumental profile and to construct artificial profiles representing doublets with separations corresponding to C^{3+} and Mg^+ . A comparison of these profiles with the observed profile is given in Fig. 2.

Table 1 Observed Lines in 1548+115a,b

Ion	Observed λ	1548+115a Rest wavelength	Equivalent width (Å)	z
Mg II	4024	2800	70	0.4382
O III ?	4496	—	4	—
He II*	—	3203	9	—
[Ne V]	4801	3346	2	0.4348
[Ne V]	4916	3426	5	0.4345
[O II]	5350	3727	5	0.4352
[Ne III]	5556	3869	6	0.4360
[Ne III]+He	5696	3968+3970	4	0.4350
Hδ	5880	4102	13	0.4335
He II*	—	4686	21	—
Hβ	6982	4861	91	0.4361
[O III]	7123	4959	18	0.4364
[O III]	7193	5007	62	0.4366
1548+115b				
Ly-α	3527	1216	224	1.901
Absorption	4038	—	12	—
C IV	4493	1549	83	1.901
C III*	5555	1909	65	1.910

Inspection shows that the absorption feature is probably due to C^{3+} .

Second, the presence of emission features close to $\lambda 4495$ in the spectra of both objects led to speculation that the C IV $\lambda_{\text{O}} 1549$ feature might be present in both objects at $z=1.901$. But the line of $\lambda 4496$ in the spectrum of 1548+115a is very probably a blend of the O III $\lambda 3122, \lambda 3133$ Bowen fluorescence lines⁷ in the $z=0.4359$ redshift system. The other lines in the O III cascade chain would be confused with the [Ne V] $\lambda 3346, \lambda 3426$ doublet and are possibly present at their expected strengths. Several other QSOs are known to have an emission line at a rest wavelength near $\lambda 3135$. Ly-α at $\lambda 3527$ does not appear in our spectrum of 1548+115a, a circumstance that strengthens the probability that the wavelength agreement between the $\lambda 4495$ features is accidental.

Finally, we note that the wavelength ratio $(1+z)_a/(1+z)_b = 2.02$. Although the observational data are sufficiently accurate to exclude the possibility that the true ratio as determined from the emission lines in the two objects is exactly 2, it would be possible for the departure from 2 to be caused by small peculiar motions associated with one or both of the objects. This difference of almost exactly a factor of two in wavelength for these two (optically) associated objects is either an unfortunate coincidence or a profound mystery.

The discovery of surprising objects such as this tempts us to make statistical arguments. Arguments about rare single events are treacherous; the archives of science are filled with dead hypotheses, supported initially by overwhelming statistical claims. One must avoid the errors of either testing only a single hypothesis, or of selecting an *ad hoc* alternative and then confirming it on the basis of the same data.

Before the observation of double QSOs, the 'most likely' hypothesis was the cosmological hypothesis: Redshifts were cosmological in origin, with a small component due to peculiar velocities. In general QSOs were expected to be randomly distributed on the plane of the sky and any groups that did appear should agree in redshift. Another hypothesis, less definite but existing before these observations, was the local

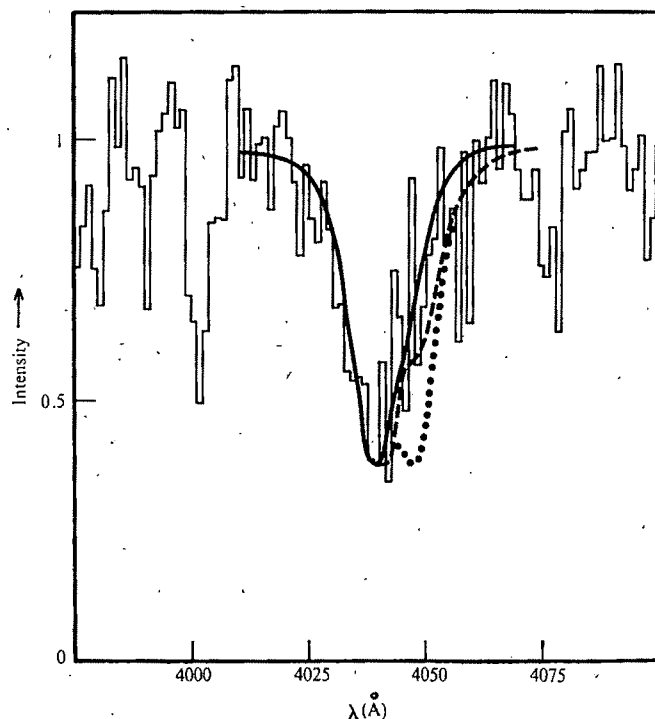
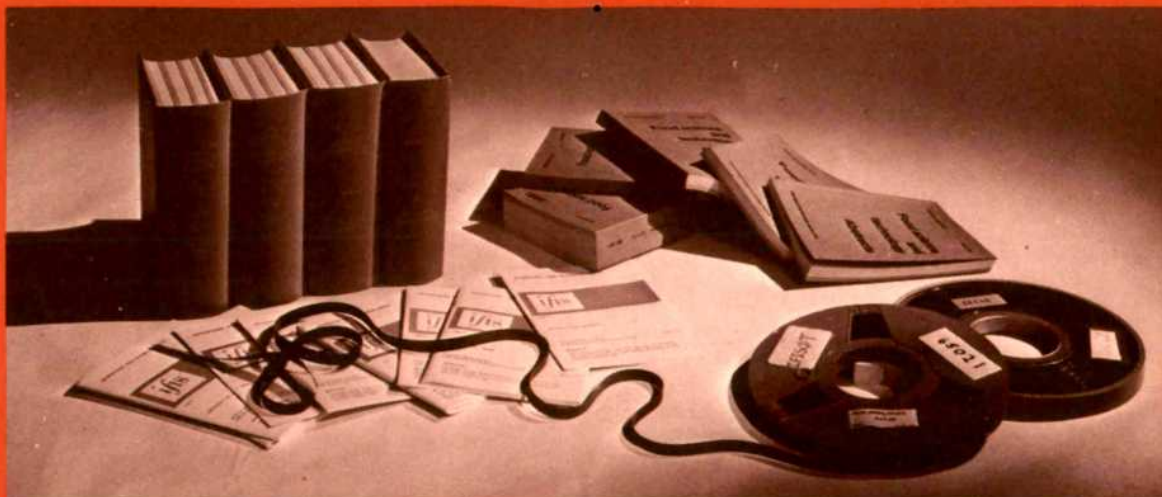


Fig. 2 The $\lambda 4038$ absorption feature in 1548+115b. The curves are computed instrumental profiles for: —, C IV $\lambda\lambda_{\text{O}} 1548.2, 1550.8$ with a 1:1 intensity ratio; ---, Mg II $\lambda\lambda_{\text{O}} 2795.5, 2802.7$ with a 2:1 intensity ratio; and ····, Mg II $\lambda\lambda_{\text{O}} 2795.5, 2802.7$ with a 1:1 intensity ratio. The night sky line Hg $\lambda 4047$ increases the

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hypothesis. The observed redshifts were allowed a large, non-cosmological, component and groups of QSOs could now have discordant redshifts.

Our observation of a close pair of QSOs with discordant redshifts is unlikely under the cosmological hypothesis. Sandage and Luyten¹ estimate that there are five QSOs brighter than magnitude 19.4 per square degree. If this is true and if QSOs are randomly distributed in the sky the chance of finding a second QSO within 5 arc s of a given object is approximately 4×10^{-5} . The probability of finding such a pair among the 250 QSOs with known redshifts is about 1 in 100 if there were no observation selection effects. Present observational techniques certainly discriminate against finding close doubles since normally the search is stopped when one candidate from a group of stars is found to be a QSO.

A local hypothesis which puts 10% of the QSOs in pairs of galactic cluster dimensions, say one minute of arc, is at a statistical advantage by a factor of thirty or so. The radio alignment, when accurately measured, may provide additional evidence. The spectral peculiarities are fascinating but no pre-existing theory suggested them and these observations only raise them for future consideration.

We believe that these observations add support to non-cosmological theories of redshifts. Such theories will receive additional support if an interaction between the two components of a close pair can be shown. Alternatively, additional close pairs may be found. Since it is now known that some large redshift QSOs have neutral colours⁸, a search for more QSO pairs should include all stars found near suspected or known QSOs.

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Discrepant Redshifts of QSOs in Clusters of Galaxies and a Close QSO Pair

ALTHOUGH it is the majority view that QSO redshifts are cosmological in origin and related to distance by Hubble's law, several workers¹⁻³ have proposed that QSOs may be more local objects. The strongest direct evidence for the conventional view is provided by observations of a number of QSOs which have been shown to have redshifts (z) which agree to within about 1% with the redshifts of apparently associated clusters of galaxies⁴⁻⁸. These QSO-cluster asso-

ciations have all been found in searches restricted to QSOs with $z < 0.36$ since on the cosmological hypothesis it is only for such low values of z that the associated galaxies would be readily visible. But, as Burbidge and O'Dell⁹ have pointed out, by assuming at the outset that the redshifts are cosmological these investigations fail to test the non-cosmological hypothesis. For the past several years we have been attempting to carry out a study of QSOs in clusters or groups which would be free from this objection. Although our results are by no means complete, we present here some of our preliminary findings as they seem to be of relevance to the present controversy.

To avoid any assumptions as to the nature of the redshifts, two of us (D. J. and C. H.) started, not with a list of QSOs, but with a list of 280 radio sources selected from the 4C catalogue and for which we had measured improved positions. The fields around each of these sources were examined on the Palomar Sky Survey Prints for possible QSO identifications, an identification being suggested whenever a blue stellar object (BSO) brighter than 19 mag was found within the error rectangle of the radio position¹⁰. In searching for possible associations with clusters we adopted the view that a QSO is typically brighter than the brightest cluster galaxies by up to 2 or 3 mag. We therefore noted all cases in which three or more galaxies lay within 1 (arc min)² of the suggested QSO identification and which on the Palomar Sky Survey E print were approximately equal to it in brightness. We noted QSOs with less than three nearby galaxies only if these were brighter than 19 mag and lay within 10 arc s. This approach not only differs from that adopted in other QSO-cluster investigations but also differs significantly from that of Burbidge *et al.*¹¹ who looked for an association between QSOs and much brighter galaxies. It assumes that the QSOs are at cosmologically significant distances rather than very local ones but not necessarily at distances given by Hubble's law.

A search was also made for situations in which more than one BSO lay close to the radio position, a few examples of this type having already been noted¹². It seemed possible that these might represent physical associations of QSOs the significance of which would be easier to establish than QSO-galaxy associations. They would therefore provide a more powerful method of investigating any possible non-cosmological contribution to the QSO redshifts, particularly if this non-cosmological component were present only in high redshift objects, say $z > 1$.

A BSO or possible BSO was found within the search area of fifty-three of the 280 sources examined. Of these fifty-three, two (4C04.54 and 4C28.40) were found to be within 1 arc min of a second BSO, three (4C24.23, 4C11.45 and 4C26.48) lay close to one or more galaxies and the sixth (4C11.50) showed both a close pair of BSOs and a galaxy within the error rectangle. The latter four cases were considered to represent the most probable associations and to be worthy of further study, the remaining forty-nine have been published elsewhere¹⁰. The adopted radio positions of the four selected sources and their position relative to the nearby BSOs are given in Table 1 and enlargements of the fields around each of the sources are shown in Fig. 1.

The most convincing case for a QSO-cluster association is provided by 4C24.23; the BSO is seen clearly near the edge of a small compact group of five galaxies which may represent the brightest members of a cluster extending over a diameter of about 2 arc min. The BSO is the brightest member of the group, consistent with it being a QSO at the same distance. The BSO identified with 4C11.45 is also the brightest member of a small compact group but both the galaxies and the BSO are some 2 mag fainter than in the case of 4C24.23. A line of three brighter galaxies within 2 arc min may be members of the same cluster. 4C26.48 and 4C11.50, each with only a single galaxy within 10 arc s, are less convincing. 4C11.50 was, however, also of par-

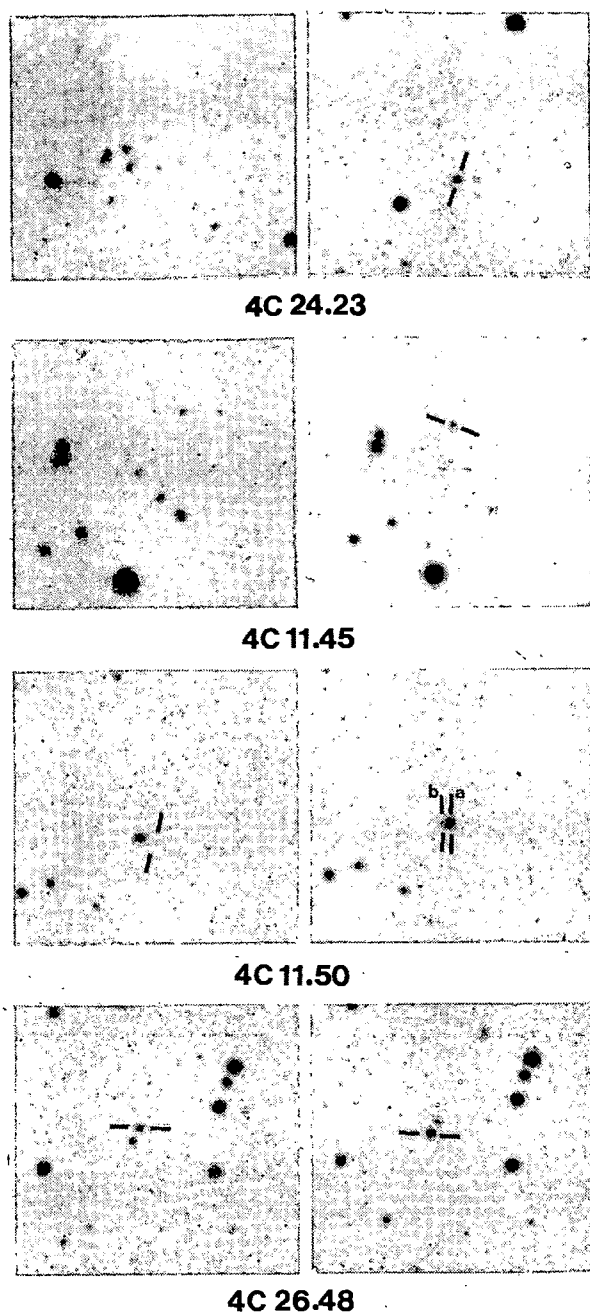


Fig. 1 Enlargements from the Palomar Sky Survey Prints of the region around the four sources, the E enlargement being on the left and the O enlargement on the right in each case. The quasistellar objects are marked on the O enlargements, and for 4C11.50 and 4C26.48 the nearby galaxies are marked on the E enlargement. Each picture is about 3 (arc min)^2 and north-east is at the top left hand corner.

ticular interest because of the presence of the two BSOs separated by only a few seconds of arc. The pair of BSOs can be clearly seen on the Palomar O plate although the fainter of the two is barely visible on the E plate which is of rather low quality. The galaxy which is visible only on the E plate is of comparable magnitude to this fainter BSO.

At this stage, because of the low accuracy of the radio positions, it was not certain that the BSOs we had noted were really QSOs rather than chance associations with blue stars. Nor could the possibility be excluded that one or more of them was a radio-quiet QSO with the radio emission originating in one of the nearby galaxies. A search of the literature showed, however, that 4C11.45 and 4C26.48 had already been suggested and confirmed as QSO identifications¹³⁻¹⁵. Since then we have taken optical spectra of

Table 1 Positions of the Four Radio Sources and the Relative Positions of the Optical Identification

Source	Adopted radio position (1950)						S_{430} f.u.	Relative position of optical identification	
	Right ascension			Declination				optical-radio "	"
	h	min	s	°	'	"			
4C24.23	10	48	46.8	24	04	18	(2.9)	0	18S
4C11.45	13	18	50.0	11	22	30	4.8	4P	5N
4C11.50	15	48	22.0	11	30	00	1.8	6P	12S
4C26.48	16	23	12.8	26	57	30	2.8	12P	12S

4C24.23 using the 200-inch telescope at Palomar and the two BSOs near 4C11.50 have been studied by Baldwin *et al.*¹⁶ at Lick Observatory. Both 4C24.23 and the fainter member of the 4C11.50 pair (4C11.50b) have been confirmed as QSOs and the brighter member of the pair (4C11.50a) was noted as having a continuum spectrum. In addition Ekers (private communication) has determined structures and accurate positions ($\pm 0.5 \text{ arc s}$) for all four radio sources using the Westerbork Aperture Synthesis array, and Fanaroff (private communication) has measured the structure of 4C11.50 using the Cambridge aperture synthesis instrument. Optical positions accurate to about $\pm 0.3 \text{ arc s}$ have been measured by Argue and by Murdoch (private communications).

A full account of these observations will be published elsewhere; at present we note that the accurate optical and radio positions confirm that for 4C24.23, 4C11.45 and 4C26.48 the radio emission does indeed originate in the QSO. The observations of 4C11.50 are particularly interesting since they show that the source is double with a separation of $\sim 15 \text{ arc s}$ in position angle 152° but with one component coincident with 4C11.50a rather than the confirmed QSO, 4C11.50b. This indicates that the source is a 3C273-type double and that 4C11.50a is also a QSO. The separation of the two QSOs is only 4.5 arc s so the possibility that they are physically associated inevitably arises. The nature of 4C11.50a has also been confirmed independently of these radio observations by Wampler *et al.*¹⁷ in a parallel optical investigation and redshifts have been measured for both it and 4C11.50b. A summary of the relevant optical information is given in Table 2.

Although the redshifts of none of the galaxies close to any of the four QSOs have been measured, we estimate from their magnitudes that they cannot in any case exceed a value of approximately 0.3. It can be seen from Table 2 that, apart from 4C11.50b, the QSO redshifts exceed this value of z to such an extent that they cannot be associated with the galaxies if the redshifts of QSOs and galaxies are both distance indicators. The possibility remains, however, that the

Table 2 Optical Data in the Suggested QSO Galaxy Association

Source	QSO magni- tude	Redshift	Notes
4C24.23	18.5	1.27	QSO in small group of galaxies
4C11.45	19	2.17 (ref. 15)	QSO in faint cluster of galaxies*
4C11.50 (a)	17†	0.43 (ref. 17)	Close pair of QSOs. 19 mag galaxy 10" preceding
	(b) 18.5	1.90 (ref. 17)	
4C26.48	17.5	0.78†	18 mag galaxy 10" north pre- ceding

* Clarke, Bolton and Shimmins¹³ have previously noted this cluster.

† The identification of 4C11.50a as a QSO has already been made by Wills and Bolton¹⁸, but neither the second QSO nor the galaxy was noted. The group of three objects has also recently been noted by Murdoch and Hazard (to be published) in an identification programme based on Molonglo radio positions.

‡ Provisional value communicated by M. Schmidt.

Table 3 Results of Counts

No. of galaxies	0	1	2	3	4	5	6	7	8	9	10
No. of (a) regions in which observed	178	90	28	1	2	1	1	0	0	0	0
No. of (b) regions in which observed	54	79	69	49	24	13	5	1	3	2	1
No. of (c) regions in which observed	22	38	40	22	6	1	0	1	0	0	0

associations are genuine but that the redshifts are not distance indicators. To support this view it would be necessary to obtain very strong evidence to rule out chance associations. In the absence of evidence showing radio or optical links to the nearby galaxies the only evidence which can be provided must be based on counts of galaxies and clusters of galaxies.

As it has been shown that the radio emission in all four examples arises in the QSO and not in the galaxies or clusters of galaxies, we need to know only the probability that out of the chosen sample of 280 radio sources four quasistellar radio sources will be found in the observed configurations; the probability of a radio-quiet QSO lying close to a galaxy need not be considered. Out of the 280 radio sources, fifty-three were suggested as possibly associated with QSOs with probably 30% representing chance coincidences with blue stars. This indicates that we are dealing with a list containing about forty QSOs which is consistent with the percentage of QSOs (~15%) usually found in source lists at the flux level of the 4C survey. The probability of two cases of a single galaxy being observed within 10 arc s of a QSO is then easily estimated from the published galaxy counts. Counts by Hoskins *et al.*¹⁹ give the probability of a galaxy above +19 mag occurring by chance within 10 arc s of a randomly chosen position as about 0.02 and hence the probability of observing two such cases in a sample of forty QSOs is about 0.3. This ignores the restriction placed on the initial survey of noting only galaxies close to QSOs when they were of comparable magnitude on the Palomar E plate. Even if this were taken into account, however, the probability could not be reduced to a significant level.

The probability that the remaining two QSOs would be observed by chance in small groups of galaxies is more difficult to assess as no figures are available for the surface density of such groups, and in any case the definition of a group is to a large extent subjective. To provide some estimate we have counted the number of galaxies seen above the plate limits in 300 randomly selected regions of sky (a) for 1 (arc min)² centred on each of the chosen points; (b) for 4 (arc min)² centred again on the chosen point; and (c) for 130 such regions we have counted the maximum of galaxies which were observed in any 1 (arc min)² not centred on the chosen point but still containing it. The results of these counts are shown in Table 3. The corresponding number of galaxies observed around 4C24.23 and 4C11.45 is shown in Table 4.

Similar numbers of galaxies would be observed by chance in about one trial in a hundred. In our random counts in most cases where the number of galaxies counted exceeded five per area, they were all at the plate limits, and with our selection criteria would not have been considered as clusters at the same distance as at least the brighter BSOs. A probability of 0.01 is therefore a conservative estimate of the chance of finding a QSO in small groups of the type we

have noted. Adopting this estimate we then find that the probability of finding two such cases in our sample is about 0.08. If the redshifts of the QSOs associated with 4C24.23 and 4C11.45 lay in the region of 0.1 to 0.3, even this probability would have led us to believe that we were dealing with physical associations and that the QSO redshifts are indeed distance indicators.

The probability is, however, too high by some orders of magnitude for our results to lend much support to the non-cosmological hypothesis. Therefore, although the possibility that the associations are genuine cannot be ruled out, the realistic interpretation is that we have simply chance associations of QSOs with small clusters of galaxies. We point out, however, that in their appearance on the Sky Survey Plates, 4C24.23 and 4C11.45 appear at least as convincing QSO-galaxy associations as those which have been used to support the cosmological hypothesis. That the only QSO-galaxy associations suggested prior to a redshift measurement should show discrepant redshifts is at least of some interest, if only to demonstrate that all possible associations do not necessarily support the conventional view.

An examination of the figures of galaxy counts presented here shows that it will be extremely difficult to establish a non-cosmological contribution to the QSO redshifts on the basis of an association with clusters of galaxies unless additional information can be obtained to rule out the possibility of chance associations. The detection near 4C11.50 of a possibly physically associated pair of QSOs seems, however, to offer a more promising approach. Assuming that these are 10⁵ radio-quiet QSOs in the sky brighter than +19 mag (ref. 20), the probability of detecting one within 5 arc s of a quasistellar radio source in a sample of forty such objects is only of the order of 6 × 10⁻⁴. In spite of their different redshifts the probability that we are dealing with a real association is therefore high, particularly as Stockton²¹ has already reported two radio-quiet QSOs separated by only 35 arc s, and which he estimates have a probability of occurring by chance of only 6 × 10⁻³. To establish beyond doubt the existence of associations of QSOs will require many more examples, preferably with more than two members, and it is to be hoped that the examples of two or more blue objects close to the position of a radio source which have already been reported^{19,23} will now be investigated optically. It may be that a significant test of the nature of QSO redshifts is at last in sight. A detailed account of the optical observations of 4C11.50 and their significance is given elsewhere by Wampler *et al.*¹⁷.

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Table 4 Number of Galaxies around 4C24.23 and 4C11.45

No. of galaxies in region	(a)	(b)	(c)
4C24.23	4	10	6
4C11.45	5	8	6

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Force on a Wire in a Magnetic Field

McCAIG¹ has suggested that a shape factor might be involved in determining the force on a current-carrying wire in a magnetic field when there is a permeability contrast between the wire and its surroundings.

Certainly, the **B** seen by the conduction electrons in the wire would then be different from that present before the wire was inserted, apparently leading to a force which depended on the wire shape and permeability as well as the current, but this then gives difficulties when considering the mutual force between two different wires carrying the same current.

The problem of the cylindrical wire with uniform current density has in fact been solved by Stratton (ref. 2, section 4.21); a simple solution of the more general two-dimensional problem is now presented and discussed. I shall show that there is no shape factor for the force in the general two-dimensional case or for an arbitrary complete circuit. There is, however, a shape factor for the torque.

For simplicity let us consider a two-dimensional equilibrium situation with all quantities independent of *z*, that is, a long straight wire in a transverse field. We wish to calculate the force per unit length required to hold the wire stationary.

The external medium is assumed to be an incompressible fluid; it is homogeneous, isotropic and linear, and has relative permeability μ_e .

Before the wire is inserted there exists a uniform field

$$\mathbf{B}_0 = \mu_e \mu_0 \mathbf{H}_0 = \mu_e \mu_0 H_0 \hat{x}$$

The medium is of sufficient extent, and the field sources sufficiently distant, that the insertion of the wire does not significantly alter the reluctance seen by the sources. Nor are the sources affected by the field of the current.

The long straight wire carries a current $I_0 = I_0 \hat{z}$. The wire can have arbitrary mechanical and electrical properties, arbitrary cross-section, and arbitrary current distribution across it provided all these are independent of *z*.

The field produced by the current will in general not be circular, and inserting the wire into the field will also distort $\mathbf{H}_0$. Outside the wire the total field **H** (strictly $\mathbf{B}/\mu_e \mu_0$) can be expressed in terms of a vector potential

$$\mathbf{H} = \text{curl}[\mathbf{T}(\rho, \lambda) \hat{z}]$$

with

$$\nabla^2 T = 0.$$

The appropriate solution for *T* is

$$T = H_0 y + a_0 \ln(1/\rho) + \sum_{n=1}^{\infty} \rho^{-n} (a_n \cos n\lambda + b_n \sin n\lambda)$$

corresponding to $H_0 \hat{x}$, a circular field $a_0 \hat{\lambda}/\rho$, and line dipole, quadrupole (and so on) fields proportional to a_n/ρ^{n+1} . Only the circular field contributes to $\oint \mathbf{H} \cdot d\mathbf{l}$ taken round a circle, so $a_0 = I_0/2\pi$, independent of the choice of origin.

The force of electromagnetic origin acting on the wire will come from both body forces (magnetic forces on the current and on the magnetisation) and surface forces (non-uniform pressure of the surrounding fluid). Fortunately it is the total force which is given by integrating the Maxwell stress over any surface surrounding the wire and entirely in the fluid (ref. 2, section 2.29):

$$\mathbf{F} = \mu_e \mu_0 \oint [(\mathbf{H} \cdot \hat{n}) \mathbf{H} - (1/2) H^2 \hat{n}] dS$$

where **H** is the total field.

Let us make the integration surface the cylinder $\rho = a$. (It is easily shown that the ends do not contribute.) In equilibrium the force cannot depend on the radius of this surface, so the only non-zero contribution to the integral must come from the interaction of the uniform field $\mathbf{H}_0$ with the circular field $\mathbf{H}_1 = I_0 \hat{\theta}/2\pi\rho$. Keeping only these terms, and remembering $\mathbf{H}_1 \cdot \hat{n} = 0$, it follows that

$$\mathbf{F} = \mu_e \mu_0 \oint [(\mathbf{H}_0 \cdot \hat{n}) \mathbf{H}_1 - (\mathbf{H}_0 \cdot \mathbf{H}_1) \hat{n}] dS$$

Performing the integration we find the force per unit length to be

$$\mathbf{f} = I_0 \mu_e \mu_0 H_0 \hat{y} = I_0 B_0 \hat{y} = \mathbf{I}_0 \times \mathbf{B}_0$$

Thus the force on the wire depends only on the total current it carries, and on the value of the uniform $\mathbf{B}_0$ present before the wire was inserted; it is independent of the shape and material of the wire, and the distribution of current in it.

Therefore the total electromagnetic force per unit length of the long straight wire is simply $\mathbf{I}_0 \times \mathbf{B}_0$. Unfortunately it does not seem possible to give a simple interpretation of this overall result in terms of the various forces acting on the wire.

To indicate the complexity of the problem, consider the much simpler situation when there is no $\mathbf{B}_0$, but only the current $\mathbf{I}_0$. One can see physically that provided the fluid has uniform permeability, and (effectively) extends to infinity, there is no reason for there to be any net force on the wire. That the net force is zero is confirmed very quickly by the Maxwell stress argument used above. However, let us consider the individual forces.

There will be induced magnetisation $\mathbf{M}(\rho, \lambda)$ in the fluid and in the material of the wire. The total field $\mathbf{B}(\rho, \lambda)$ can be expressed as $\mathbf{B} = \mathbf{B}_f + \mathbf{B}_i + \mathbf{B}_e$, where $\mathbf{B}_f$ is that field which would be given by the current I_0 in free space, $\mathbf{B}_i$ that from the (internal) wire magnetisation, and $\mathbf{B}_e$ that from the (external) fluid magnetisation.

The resultant body force on the wire will come not only from the integral of the Lorenz force $\mathbf{j}_0 \times \mathbf{B}$, but also from the integral of the force $(\mathbf{M} \cdot \nabla) \mathbf{B}$ exerted on the wire magnetisation by the gradient of **B**. Many of the contributions must cancel on integration, because they correspond to the 'action' and 'reaction' of forces between different parts and properties of the wire, but two terms are left. These are the volume integrals of $\mathbf{j}_0 \times \mathbf{B}_e$ and $(\mathbf{M} \cdot \nabla) \mathbf{B}_e$, both involving the field whose source is the (non-uniform) magnetisation of the surrounding fluid.

In addition to these body forces there will also be a surface force given by the integration of the (non-uniform non-

isotropic) fluid pressure of magnetic origin; this third term also derives from the non-uniform magnetisation of the fluid. (Any hydrostatic pressure of gravitational origin will, for our incompressible fluid, be unaffected by the presence or absence of magnetic fields.)

The total force is, however, zero. Therefore either the integrated effects of the three terms are individually zero or the three effects are non-zero but cancel. That the forces are individually zero is reasonable for simple geometries but most unlikely for arbitrary geometry, so, even in this apparently simple situation, in general there must be a complicated balance between the body forces and surface forces which arise from the magnetisation of the fluid.

In the more general case with a $\mathbf{B}_0$ there must be an even more complicated partial balance between the three types of force ($\mathbf{j} \times \mathbf{B}$, $(\mathbf{M} \cdot \nabla)\mathbf{B}$, and surface pressure), and one can only be thankful that the Maxwell stress approach avoids the need to calculate them individually.

The net result is, however, that, in this two-dimensional situation in a given fluid, long straight wires of whatever material or cross section carrying the same current experience the same force; there is no need for a shape factor, as suggested by McCaig¹. (He was, however, correct in suggesting that the solution to his problem might lie (partly) in pressure surface forces.) (If $\mathbf{B}_0$ is in fact produced by, say, a parallel wire in a different medium, then the forces on the two wires are not equal and opposite, but the difference is the force required to keep stationary the boundary between the two media.)

Whatever the details of the force balance which leads to this simple result in the two-dimensional case, there is no guarantee that the same balance will hold in more complicated geometries. Nor can the Maxwell stress approach then be used, because it is no longer possible to integrate over a surface (effectively) entirely in the fluid. The force on a complete circuit can, however, be determined.

In fact there is no net force on a complete circuit in a uniform $\mathbf{B}_0$. (This can be seen by integrating the Maxwell stress over a spherical surface enclosing the circuit; by the same type of argument as used above, the only type of field of internal origin which can give a non-zero force by interaction with the uniform $\mathbf{B}_0$ is that of a monopole.) We can therefore say that the two-dimensional result that the force on a wire does not contain a shape factor is valid also for the (zero) force on a complete circuit.

Although plausible, it has not been shown that the result holds for any portion of a circuit.

Although the force on a straight wire or complete circuit has been shown to be independent of shape and of permeability contrast, this is not true for the torque. Even in the two-dimensional case, any line-dipole field produced by the wire will give a torque; although the current itself cannot directly produce such a field it can induce a net line-dipole moment in any asymmetric permeability contrast.

In the more general situation of a complete circuit this contribution to the torque still exists, but there will now be other, probably larger, contributions. Consider, for example, a rectangular coil; the wire on one side of the coil will be magnetised by the field of the current in the opposite side, and will give an additional dipole moment, and hence torque, which will depend on the permeability contrast between the wire and the fluid.

McCaig's discussion was prompted by the experiment of Whitworth and Stopes-Roe³. They adjusted the current in a coil until the torque on the coil balanced the torque on a permanent magnet fastened to the coil, when both were immersed first in water and then in a paramagnetic fluid. In fact a rough estimate shows that the above effect would reduce the current change by about 5%.

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Evidence for the Opening of the South Atlantic in the Early Cretaceous

ONE of the cornerstones of continental drift is the fit¹ of the continental edges of Africa and South America by removal of the South Atlantic Ocean, which is thought to have formed by the rifting of these two continents some time in the Mesozoic and their subsequent drifting apart. We shall present evidence from marine magnetic anomalies in the southern South Atlantic that demonstrates that this initial rift first occurred in the early Cretaceous, probably in the Valanginian (~125 to 130 m.y. BP). This conclusion is based mainly on a magnetic lineation pattern that lies in the Cape Basin directly south-west of the continental edge of South Africa, although we very tentatively identify a few of the same anomalies on the other side of the ridge in the Argentine Basin.

West of Cape Town, South Africa, in the Cape Basin, there occurs a sequence of north-west trending magnetic anomalies which indicates that seafloor spreading took place from 130 to 110 m.y. BP (Fig. 1). In the Argentine Basin, possible correlative anomalies are identified, though their definition in the Argentine Basin is poorer than in the Cape Basin. As can be seen in Fig. 1, the anomalies (which we will call the Cape sequence) can be traced in the Cape Basin from 34° S to 40° S. A lack of properly oriented track lines prevents identification further south. Track lines immediately to the north of 34° S, though properly oriented, do not show the anomalies.

To the west of the lineated anomalies, the magnetic field is characterised by irregular, low amplitude anomalies which do not correlate from track to track. One has to go west to 4° E before encountering the lineated anomalies of the late Creta-

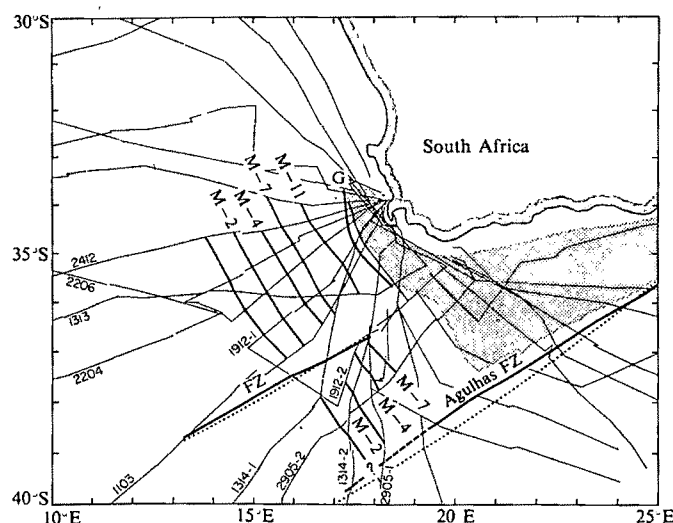


Fig. 1 Magnetic lineation chart of the Cape Basin off South Africa. Mesozoic magnetic lineations are labelled M. Lineation labelled G is the edge of the African continent defined by a steep gravity gradient by Talwani and Eldholm². The stippled pattern is an area of very small magnetic anomalies that corresponds to the submarine portion of the African continent³. Mapped fracture zones are shown with bold, solid or dashed lines. Synthetic fracture zones drawn as small circles about the pole of early opening⁹ are shown with dotted lines. Ship tracks are thin, solid lines. Magnetic anomaly data collected on the

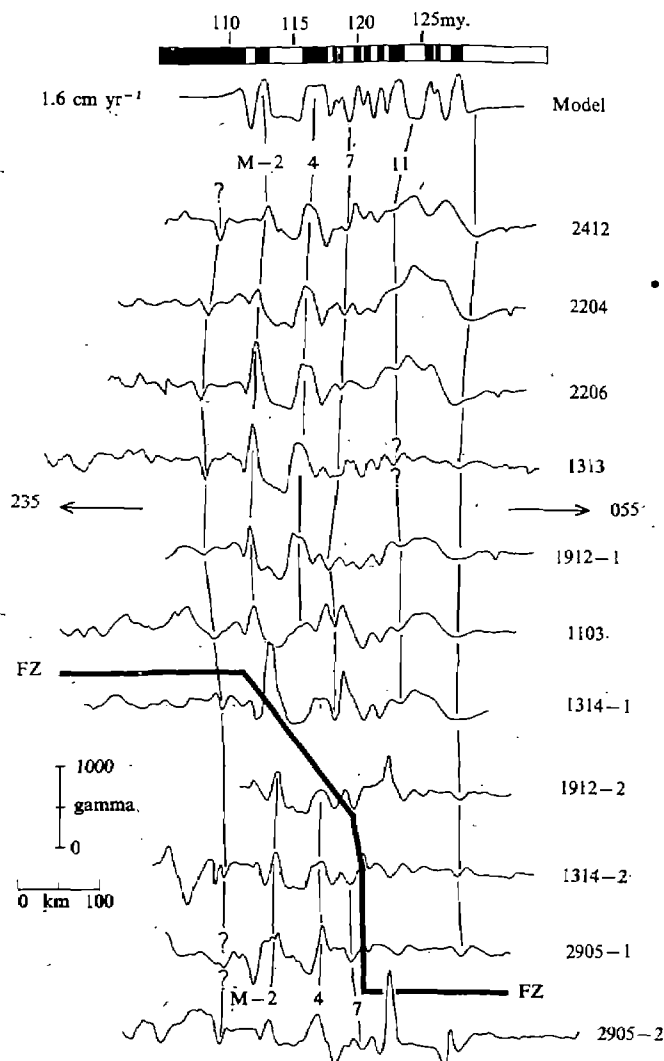


Fig. 2 Magnetic anomaly profiles across the Cape Basin lineations shown projected to a direction perpendicular to the structure. FZ is the small fracture zone offset shown also in Fig. 1. M lineations are from Larson and Pitman⁵. The magnetic block-model was made by combining the Mesozoic reversal time scale⁵ with a spreading half rate of 1.6 cm yr⁻¹. The direction of remanent magnetisation is inclination=60° up, declination=30° W, in accord with a palaeomagnetic pole location for Mesozoic Africa at 65° S, 82° E (ref. 6).

ceous-Cainozoic reversal sequence which cover the mid-ocean ridge. Northward the Cape sequence trends into the marginal smooth zone defined² on the basis of aeromagnetic data. In the area of the Cape sequence, the aeromagnetic data reveal a sequence similar to that derived from the ship data used here. We do not show aeromagnetic data because the positions of magnetic anomalies so determined are offset several miles with respect to ours, and thus we suspect that the aircraft navigation is slightly in error.

To the east, the Cape sequence borders the continental margin as defined by Talwani and Eldholm³ using gravity and magnetic data. They suggested that the boundary between oceanic crust and continental crust is marked by a steep gradient in the isostatic gravity anomaly that lies at the edge of the continental structure. This gradient is nearly coincident with a change in the magnetic signature from a smooth, almost featureless magnetic field over the continental shelf and upper slope seaward to a region characterised by relatively large amplitude anomalies similar in magnitude and width to recognised seafloor spreading anomalies. It is these anomalies seaward of the upper continental slope that we have correlated with early Cretaceous anomalies recognised in the North Atlantic and North Pacific^{4,5}.

The correlations can be seen in Fig. 2 where the magnetic data were projected from several ship tracks on to a line trending N 55° E. At the top of Fig. 2 is a model computed using the Mesozoic reversal sequence⁵ determined by correlating the Mesozoic lineations in the North Pacific with the Keathley sequence in the North Atlantic. A mean Mesozoic palaeomagnetic pole at 65° S, 82° E (ref. 6) was used to determine the remanent magnetic direction for the model.

We consider the correlations, both from track to track and with the model, of anomalies M-1 to M-5 to be excellent. Note especially the well developed and well reproduced shapes of anomalies M-3 and M-4 and the spacing of anomalies M-2, 3 and 4. Anomalies M-6 and M-7 are usually present as modelled, but the lineation of the anomalies older than M-7 and their comparison with the model is often poor. We attribute at least some of this poorer correlation to disruption of the lineation pattern by the initial rifting phenomenon and point out that our identification of these anomalies as an expression of the Mesozoic reversal pattern rests almost wholly on evidence from the younger portion of the sequence. The oldest anomaly (Fig. 2) next to the continental edge is a well lineated negative feature that could be M-13, or the edge of the African continent³. Our model shows it as a reversal, but a non-magnetic (continental) block at this point would not change the shape appreciably.

The most disturbing part of this interpretation is the negative magnetic lineation that always occurs to the west of (younger than) anomaly M-1 (Fig. 2). This anomaly does not consistently occur in this position with respect to other Mesozoic lineation sequences^{4,5} although three negative lineations have been correlated⁷ east of (younger than) the Keathley sequence that may be related to the Bermuda Discontinuity. If our interpretation of these lineations in the Cape Basin as Mesozoic magnetic anomalies proves correct, it will be necessary to introduce another reversal into the magnetic time scale that is just younger than M-1.

A slight offset in anomalies M-1 to M-7 south of line 1314-1 indicates a fracture zone. On checking the seismic reflection profiler records, we were able to find additional evidence of a fracture zone in the area suggested by the magnetic lineations. The fracture zone shows up as discontinuities in basement topography, particularly as basement peaks. The peaks appear in the magnetic data as large, isolated, positive anomalies on tracks 1103 and 1314-1. This fracture zone parallels the Agulhas Fracture Zone^{3,8} to the south that appears in magnetic data as a large positive peak that parallels the south-east edge of the Agulhas plateau. In Fig. 1 we have drawn for comparison synthetic fracture zones about the early opening pole based on fracture zones in the central Atlantic⁹. The trends of the synthetic fracture zones are nearly identical to the trends of the two observed fracture zones. The fact that the trends of these fracture zones match the synthetic trends is additional evidence that offsets and lineations of the continental margins have recorded the directions of motion during the early opening⁹. In particular, the Agulhas Fracture Zone is the African counterpart of the Falkland Plateau scarp, a conclusion that was reached more qualitatively by observation of the trend of the south-eastern edge of the African continent by Francheteau and Le Pichon¹⁰, and by observation of a buried marginal ridge on the south-east side of the Agulhas Plateau by Scrutton and du Plessis³.

In the western Argentine Basin magnetic anomalies for the most part are subdued and display no coherence from track to track; however, four tracks from the Lamont data library over the lower continental rise off Argentina display two large positive anomalies that are consistent from track to track. There also seems to be a left lateral offset in the anomaly lineation pattern. The spacing is similar to anomalies M-2 to M-4 of the Cape sequence. Also, they are at about the same latitude relative to the pole of rotation as the Cape sequence, lie about the same angular distance from the continental slope as M-2 to M-4 in the Cape Basin, and their spacing shows the

same half-spreading rate. The above observations taken together indicate that some of the Mesozoic anomalies of the Cape sequence are also present in the Argentine Basin. We do not understand why they are not as well-developed in the Argentine Basin. Model studies indicate that the greater depth to basement (~ 8 km) in the Argentine Basin will not attenuate the anomalies as much as observed.

Assuming that our anomaly identifications in both the Cape Basin and the Argentine Basin are correct and accepting the Talwani and Eldholm³ analysis of the continental margin west of Cape Town, a consistent picture is obtained by drawing the ocean basin and continents as they were at the time of formation of anomaly M-2. If the ocean is closed completely using the rotation to the 500-fathom line, a large (~ 100 km) gap is left open west of Cape Town. The extension of the African continent westward of the 500 fathom line as suggested by Talwani and Eldholm³ partially fills this gap.

Using the early opening pole⁹, we rotated anomaly M-2 of the Cape sequence back to the continental edge as defined by Talwani and Eldholm³. An angle of 2.3° is necessary for this rotation. This angle will represent half the motion of South America with respect to Africa between the initial rift and anomaly M-2. If South America, together with anomaly M-2 from the Argentine Basin, is rotated westward from the 500-fathom fit to Africa¹ by 4.6° (twice 2.3°) about the early opening pole⁹, the anomalies M-2 of the Argentine Basin nearly coincide with anomalies M-2 of the Cape Basin (Fig. 3). It is also apparent (Fig. 3) that the proposed left-lateral offset in the Argentine Basin then corresponds in position, sense and amount of offset with the small fracture zone that we identify in the Cape Basin.

Thus, our identification of the Mesozoic anomalies on both sides of the South Atlantic, Talwani and Eldholm's³ definition of the edge of the continent west of South Africa, and the 500-fathom average fit of the entire South American and African margins¹ are internally consistent. This suggests that the 500-fathom line may be a good average definition of the edge of the continent though locally (in the Cape Basin) there are deviations from this average.

Larson and Pitman⁵ did not recognise these Mesozoic magnetic lineations in the Cape and Argentine Basins and thus suggested that the South Atlantic did not begin to open until, or subsequent to, 110 m.y. BP. Our identification of these anomalies corrects this suggestion, but does not appreciably change their calculation of the rate of rapid spreading in the South Atlantic from 85 to 110 m.y. BP. It seems to lower the rate for that period by about 10%; for instance, at 40° S latitude the rate drops from about 5 to about 4.5 cm yr^{-1} . For the time period 110 to 127 m.y. BP the spreading rate is 1.6 cm yr^{-1} (see Fig. 2).

Figure 3 shows a reconstruction of Africa and South America at 112 m.y. BP (anomaly M-2 time) accomplished by the rotations just described. The relative proximity of the pole of rotation (21° N, 14° W)⁹ resulted in the early opening up to at least 112 m.y. BP occurring somewhat as a scissors-type motion. The lineations in the southern South Atlantic were generated in accord with motion at that latitude, while the northern South Atlantic remained more nearly closed. The close proximity of northern South America to northern Africa until at least 110 m.y. BP is in accord with palaeontological and stratigraphical studies in Brazil and Gabon that show freshwater lake deposits near or at the rifted coastlines throughout the Neocomian (~ 135 to 112 m.y. BP)^{11,12}. These were followed in the Aptian (~ 112 to 105 m.y. BP) by salt deposits in the same approximate locations^{11,13,14}. Because there is little motion between northern Africa and northern South America, it is not obviously necessary to resort to forming these deposits behind dams that cut off the southern Neocomian and Aptian Seas, although the Walvis Ridge and Rio Grande Rise could have acted as such structures (R. Leyden and J. R. Nunes, to be published). Finally, by Albian time (~ 105 to 100 m.y. BP) a wide, shallow marine transgression occurred

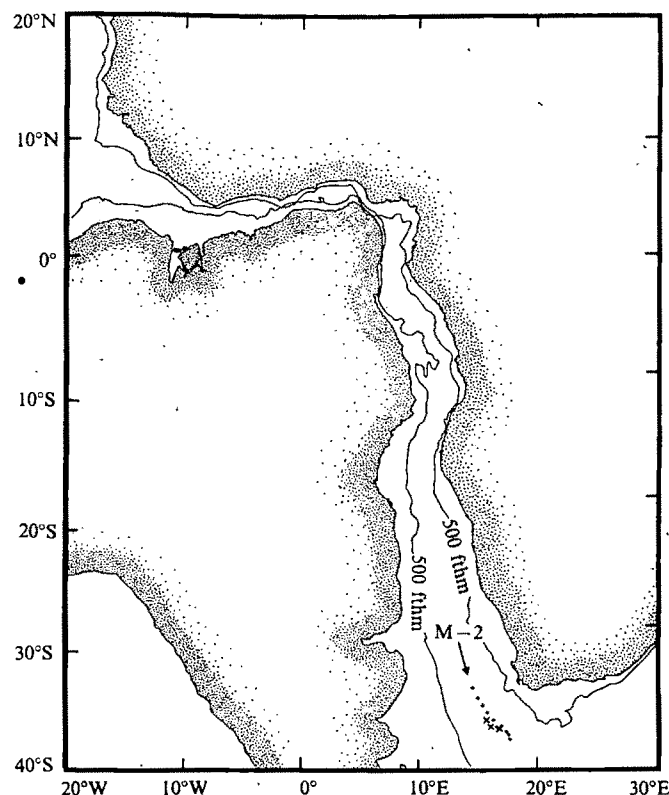


Fig. 3 Palaeogeographical reconstruction of the South Atlantic at 112 m.y. BP (anomaly M-2 time). The reconstruction was made for Africa and the Cape Basin lineations (+) in their present positions by rotating South America and the Argentine Basin lineations (x) first by $+57.0^\circ$ about a pole at 44° N, 30.6° W (ref. 1), and then by -4.6° about a pole at 21.5° N, 14° W (ref. 9). These manipulations bring the M-2 lineation of the Argentine Basin into near coincidence with the M-2 lineation of the Cape Basin.

and the northern South Atlantic was completely open for the first time¹¹.

The oldest magnetic lineations in the Cape Basin are also in close agreement with the ages of the Serra Geral basalts in Brazil that date the initial rifting in that region at 120 to 130 m.y. BP¹⁵ and the Kaoko basalts of south-west Africa whose radiometric age is 114 to 130 m.y. BP¹⁶. The age of the oldest magnetic lineations (~ 127 m.y. BP, anomaly M-12) is also coincident with the marine transgression of southern Africa, southern Chile, and southern Argentina during the Upper Valanginian (~ 127 to 124 m.y. BP)¹². It seems to us that this marine transgression is the direct result of the pattern of early rifting described above. Hallam¹⁷ and Reymont¹¹ studied the palaeontological associations of Lower Cretaceous formations of South America and Africa and concluded that there is enough similarity of the faunas to demonstrate that only a narrow seaway separated Africa from South America during the Neocomian. The Upper Valanginian marine transgression suggested to Reymont and Tait¹² that this was the time that the land masses began to drift apart. Fossil evidence along the south-east coast of Brazil and the western coast of Africa indicates that by Upper Aptian time an arm of the sea had extended northward at least as far as Sergipe and Gabon. The distribution of nektonic ammonite shells indicates that the North and South Atlantic were finally joined in the Lower Turonian, as land connections between Africa and South America in equatorial regions were severed.

We agree that during the Valanginian only a narrow seaway separated Africa from South America because that is the age of M-12, the anomaly that dates the onset of continental drift. We speculate that the Valanginian was not only the time of the initial opening of the South Atlantic, but also of the more

general breakup of Gondwanaland. As the nearest pole of rotation lies to the north, the spreading rate on the ridge that created the Cape Basin lineations must have increased towards the south. Thus, somewhere south of the Cape Basin this ridge met a triple junction, or was transformed to another spreading centre with a faster rate. It is unlikely that the ridge could have been transformed between Antarctica and South America into the Pacific because the Palaeozoic and Mesozoic formations on these continents form continuous sequences that were not fragmented into the Scotia Arc until at least the end of the Andean Orogeny in the Cainozoic¹⁸.

Thus, the ridge was probably transformed to the east into the newly forming Indian Ocean or between the two stable masses that now form east and west Antarctica. The former suggestion is similar to that made by McKenzie and Sclater¹⁹ for the plate boundaries in this area from 75 to 55 m.y. BP. It is an hypothesis that awaits testing by determining the presence or absence of the Mesozoic lineation pattern at the stable margins of the Indian Ocean.

We thank Manik Talwani and Olav Eldholm for pointing out to us the existence of magnetic lineations in the Cape Basin. This research has been sponsored by the US Office of Naval Research and by a grant from the Oceanography Section of the National Science Foundation to the Lamont-Doherty Geological Observatory.

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World-wide Source of Leaf-derived Freezing Nuclei

INITIATION of precipitation over much of the Earth's surface is believed to be intimately related to the development of ice in supercooled clouds. The source, composition and number of small particles (ice nuclei) initiating freezing events in natural clouds are poorly understood. These particles represent a very small fraction of the total aerosol in the atmosphere. The material most frequently held to

represent the majority of ice nuclei are clays, especially kaolin.

In a summary of earlier research, we reported^{1,2} that decomposed plant leaf litters contain large numbers of freezing nuclei and that these nuclei are perhaps responsible for the nucleating abilities of soil particles. (Freezing nuclei are defined as particles capable of nucleating ice in supercooled water. If no distinction is made between freezing and deposition the nuclei are referred to as ice nuclei.) The leaf-derived nuclei (LDN) were found to initiate freezing of supercooled water drops at temperatures warmer than -5°C and to occur in concentrations of up to 10^{10} nuclei active at -10°C per g of decaying leaf. The conclusion that the nuclei are products of decomposition was reached by following the decay of fresh leaves in the laboratory and observing the gradual evolution of nuclei to the stage comparable to naturally decomposed litters. (Extensive chemical analyses have not yet revealed the structure of the LDN but indicate that the nucleating particles probably constitute less than 0.1% of the total decayed leaf litter mass. Filtration tests suggest that the LDN particles are between 0.1 and $0.05\text{ }\mu\text{m}$ in diameter. Heat in excess of 60°C deactivates the nuclei, supporting the suggestion that they are organic in nature.) Though it has not yet been shown that the mechanisms transferring LDN to the atmosphere are of sufficient intensity to account for atmospheric ice nucleus concentrations, it was felt important to establish the extent to which LDN are available on a global basis.

We collected samples of well decayed litter from fifty different dominant tree or grass species across the northern hemisphere. The sampling locations were spread throughout North America, from the Pacific to the Atlantic, and across Europe and northern Asia from Britain eastward through Siberia to Japan. A second set of samples was collected along a transect from Japan through southeast Asia into western India.

Testing of the little samples for freezing nucleus content was done in a standardised manner by inserting 1 g (dry weight) of leaf material into 100 g of distilled water followed by agitation and a 5-min settling period. The resulting suspension was filtered through a paper filter with a pore size of approximately $50\text{ }\mu\text{m}$. The slightly turbid filtrate was tested on a nucleus spectrometer following the principles and procedures outlined by Vali³.

Numerous samples were found to contain freezing nuclei in numbers comparable with what has been reported earlier². Some other samples were found to contain fewer ice nuclei, by factors of up to 10^5 . The abundance of nuclei in a sample appeared not to be correlated with species but showed a closer similarity to samples from the same geographical location. On closer analysis it became apparent that nucleus content is closely related to the climate prevailing at the sample's origin, almost regardless of the species of plant.

According to Köppen⁴, the Earth is divided into six principal climatic zones depending on seasonal temperature and variation, precipitation pattern, and physiography. Of the six zones, three have extensive vegetation (A, tropical; C, humid mesothermal; D, microthermal) and the remaining three have lesser amounts of vegetation (B, dry; E, polar; H, undifferentiated highlands). The type of vegetation growing in each climatic zone is very distinctive for that zone. Data are presented in Fig. 1 for three climatic zones for which a minimum of twelve nucleus spectra per zone is available. For each climatic zone, the highest, lowest and median spectra are plotted. A clear separation between the three zones is evident.

Samples of the genus *Poa* were collected from each of the climatic zones A, C and D. The nucleus contents of the three samples were found to coincide with the typical spectra for each of the zones. Samples of the genera

Fagus, *Oryza*, *Populus* and others were available from two of the climatic zones. In each case the nucleus content followed the climatic trend. Thus, ice nucleus content can be clearly seen to depend primarily on the climate of a sample's origin; it is also evident that the range of nucleus contents for samples from a given zone is quite restricted.

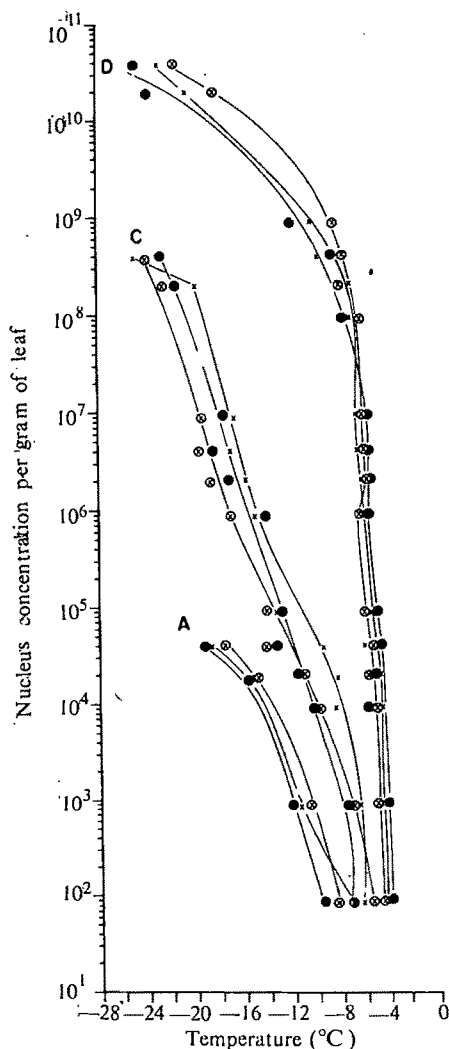


Fig. 1 Freezing nucleus spectra of well decayed leaf litters from A, C and D-type climate zones. For each zone, the highest, lowest and median spectra are plotted.

What factors cause the close tie between nucleus content and climate of growth? Since the process of formation of the freezing nuclei from leaf matter is not yet known, the reasons can only be speculated upon. It is known in general that decomposition is mediated by bacteria and the specific role of bacteria in producing freezing nuclei from leaf matter was demonstrated by Fresh⁵. Differences in microflora among climatic regions might thus be one of the factors. Others of possible importance are the availability of moisture, average air temperature and type of soil substrate.

The climatic dependence of freezing nucleus content in leaf litters does not make itself evident in the concentrations of airborne ice nuclei which have been found to be fairly constant globally⁶. Atmospheric mixing and the possibility that the release of nuclei from litters may also be variable with climate, in an inverse way compared with the availability of nuclei, may account for the observations.

In summary, the world-wide availability of LDN

strengthens the suggestion that LDN may constitute a significant fraction of the atmospheric ice nuclei.

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BIOLOGICAL SCIENCES

Rapid Screening Assay for Revertants derived from MSV-transformed Cells

MURINE sarcoma virus (MSV)-transformed 3T3FL cells (S⁺L⁻ cells¹) produced spontaneously and at variable rates flat variants (revertants) from which MSV could no longer be rescued by superinfection with murine leukaemia virus (MuLV)^{2,3}. During the course of investigation of reversion frequency in S⁺L⁻ cells, we have been able to detect revertants by a rapid screening assay technique instead of using the more cumbersome cloning procedure in microtitre wells as previously described^{2,3}. The S⁺L⁻ cell line 3197¹⁻³ was composed of hyper-refractile, loosely attached cells and did not form a compact cell monolayer. Infection of this cell line with MuLV changed the cellular morphology to a slightly more rounded cell type, and increased the tendency of cells to detach readily from the surface of the container. When rescue-negative revertants derived from S⁺L⁻ cells were infected with MuLV there was no observable change in cellular morphology. These characteristics can be used as the basis for a rapid screening assay technique for revertants from S⁺L⁻ cells, the details of which are described here.

The sublines of 3197 cells, 3-321 and 3-360 (ref. 4), grown in modified McCoy's 5a medium with 10% foetal calf serum (Grand Island Biological Co.) were infected with the IC isolate of Moloney leukaemia virus⁵ at MOI > 5 focus inducing units (FIU)⁶, and 1,000–5,000 cells in 5 ml medium were delivered into 25 cm² flasks (Falcon). Flasks were incubated at 37° C for 4 d, then shaken to detach the relatively loose S⁺L⁻ cells; supernatant was removed and flasks were washed twice with medium. Five millilitres of fresh medium were added and flasks were further incubated at 37° C. After a further 3–5 d of incubation, flat, contact-inhibited revertant cell colonies formed and were counted. When S⁺L⁻ cells were infected with MuLV at high MOI (> 5 FIU), MSV was rescued from them about 12 h after infection⁷. At that time, viral interference had developed in rescue-negative revertant cells following MuLV infection, and no transformation of revertants was produced by the rescued MSV. Therefore, revertants remained flat and formed colonies.

The sensitivity of this technique in the detection of revertants was compared with that of cloning techniques^{2,3} in which flat cell colonies were isolated in microtitre wells (Micro Test II tissue culture plate, Falcon) and then tested for rescuable MSV genome by superinfection with MuLV^{1-3,7}. Quantitatively, these two assays gave results which were in close agreement, with the following reversion frequencies: 0.0002 and 0.0003 in 3-321 cultures, and 0.003 and 0.005 in 3-360 cultures, as can be seen in Table 1.

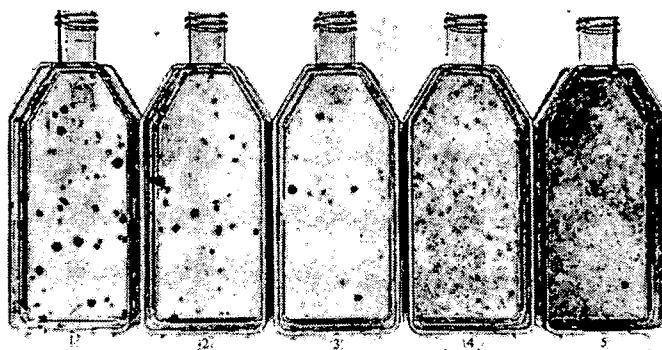


Fig. 1 Reconstruction experiment. Mixtures containing 200 (1), 100 (2), 50 (3), 200 (4) and 0 (5) MSV-revertant cells plus 10,000 S⁺L⁻ cells were seeded into flasks and (1), (2) and (3) were simultaneously infected with MuLV. On day 4, cultures (1-3) were shaken, washed and refed. Photographs were taken after staining on day 9.

The reliability of the rapid screening assay technique for revertants was assured by the following reconstruction experiment. Mixtures containing 400, 200, 100, 50 and 25 revertant 3D-2-14 cells³ plus a constant number (10,000) of 3-321 cells were distributed into flasks, four per group, in the presence or absence of MuLV. At 4 d, cultures were shaken, washed and refed as described above. On day 9, cultures were fixed and stained with Giemsa, and colonies of revertant cells were counted. The average number of revertants in the infected groups was 186, 100, 48.3, 24.5 and 10, respectively. Some stained cultures are shown in Fig. 1. An average cloning efficiency of all groups was 47% which was similar to that of 3D-2-14 cell alone (42%). In uninfected flasks, colonies were small and fewer colonies ($\frac{1}{4}$ the number in the infected group) were observed. This seemed to result from an interference with the growth of the revertants by an excess of S⁺L⁻ cells. These findings, nonetheless, indicated that the rapid screening assay technique allowed detection of revertant colonies in mixed populations containing a large excess of transformed cells.

This rapid screening assay procedure is not only useful for determination of the spontaneous reversion frequency in S⁺L⁻ cells, but is also valuable for the study of the effects on MSV-transformed cells of physical, chemical and biological agents which enhance the frequency of reversion⁴. Two million 3-321 cells, whose reversion frequency was lower than 0.0003, were exposed to 20 ml of medium containing various concentra-

tions of fluorodeoxyuridine (FUdR) for 1 h at 37° C. At the end of the exposure period, medium containing FUdR was removed, cells were washed twice with medium and dispersed, and 100 cells were plated into 60×15 mm plastic plates (cloning technique), or 1,000 cells were delivered, in the presence of MuLV (MOI>5 FIU), into flasks for rapid screening assay. More than ten plates or flasks were used for each concentration of chemical. On day 8, flasks were examined for the presence of revertant colonies. The results of dose-response in the derivation of revertants from S⁺L⁻ cells are presented in Fig. 2; the optimum dosage of FUdR was 15 μ g ml⁻¹ which produced a reversion frequency of 0.008, and the same efficiency of revertant detection was found by both techniques. Accordingly, FUdR can be considered as increasing the spontaneous reversion frequency by about thirty-fold. The observed decrease in reversion frequency by high concentrations of FUdR cannot be explained solely on the basis of reduction in cloning efficiency⁴.

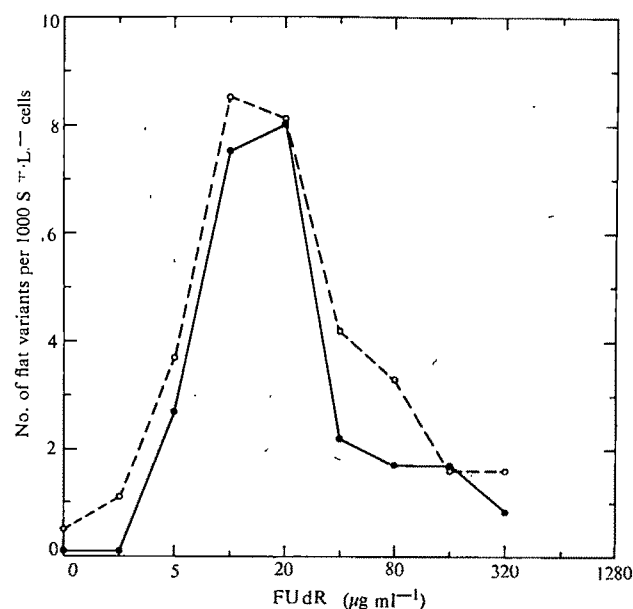


Fig. 2 Dose-response of FUdR in the induction of revertants from S⁺L⁻ cells. S⁺L⁻ cells were treated with various concentrations of FUdR for 1 h at 37° C. At the end of the exposure period, cells were washed and plated at a concentration of 100 cells per plate for cloning technique (●) or 1,000 MuLV-infected cells per flask for rapid screening assay technique (○). On days 7 to 9, frequencies of revertants were determined.

Table 1 Comparison of Sensitivity of Detection of Revertants from S⁺L⁻ Cells by Cloning and Rapid Screening Assay Technique

S+K ⁻ subline	Assay technique	No. of cells plated	No. of revertants*	Average frequency
3-321	Cloning	Microtitre wells†		
		1,000	0	
		800	0	
		500	0	0.00018
	Plates‡	12,500	3	
		1,100	0	
		500	0	
3-360	Rapid screening	51,200	11	
		16,000	4	0.00026
		10,000	5	
	Cloning	Microtitre wells		
		200	1	0.005
	Rapid screening	400	2	
		10,000	33	0.0033

* Flat and rescue-negative.

† Plates 0.2 ml of cell suspension containing 1 cell ml⁻¹.

‡ Because of their low reversion frequency, cells were seeded into plastic plates (60×15 mm) at a concentration of 100 cells per plate. On day 9, flat cell colonies were isolated and recloned in microtitre wells.

Preliminary data with Kirsten MSV nonproducer Balb/3T3 cells⁸ similarly demonstrated that the reversion frequencies of a rescue-negative revertant were 0.001 by the cloning technique and 0.0009 by the rapid screening assay procedure. Another subline of S⁺L⁻ cells, FG-10 (refs 1 and 2), revealed reversion frequencies of 0.02 by both procedures.

In summary, the rapid screening assay procedure is a simple and convenient method for the detection and quantitation of MSV-revertants, and is comparable in sensitivity to the cloning technique. It may also prove useful for the investigation of the reversion effects of a variety of agents on transformed cells.

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Prostaglandins as Potentiators of Increased Vascular Permeability in Inflammation

PROSTAGLANDINS are released in inflammatory reactions in animals¹ and in man². The observation that non-steroidal anti-inflammatory agents inhibit prostaglandin synthesis *in vitro*^{3,4} and *in vivo*⁵, and that the comparative potency of these anti-inflammatory compounds is the same *in vitro* and *in vivo* as inhibitors of carrageenin-induced oedema⁶, suggests that prostaglandins may have an important role in inflammation. Prostaglandins (E₁, E₂, F_{1a} and F_{2a}) evoke increased vascular permeability in the skin of rat and man⁷, which appears to be an indirect effect resulting from mast cell degranulation. The lack of potency of prostaglandins in causing increased vascular permeability on intradermal injection in the guinea pig⁸ has, however, received little attention. We have confirmed this observation (Fig. 1, Table 1) and conclude that in the guinea pig prostaglandins cannot be regarded as chemical mediators which act directly on the vascular endothelium as do histamine, serotonin (5-hydroxytryptamine) and bradykinin. We have therefore investigated a possible alternative role for prostaglandins in inflammatory mechanisms.

The widespread occurrence of prostaglandins in animal tissues together with their mode of action on a wide range of physiological systems has led to the proposition that these substances may have a general function as modulators of cellular responses to a variety of stimuli⁹ (for example, to hormones, neurosecretions, neural transmitters and electrical stimulation). Examples of physiological systems in which prostaglandins may act as modulators include: fatty acid and glycerol production by the epididymal fat pad in response

to adrenocorticotrophic hormone (ACTH) or glucagon¹⁰; altered permeability to water in the toad bladder in response to vasopressin¹¹; gastric secretion in the rat in response to pentagastrin¹²; smooth muscle contraction in response to sympathomimetic amines¹³, and transmitter release from pre-synaptic nerve terminals following stimulation of the splenic nerve¹⁴. An analogous situation is that of cutaneous pain in man where prostaglandins in conjunction with agonists were shown to induce hyperalgesia and overt pain¹⁵. We have therefore investigated the possibility that prostaglandins may act as modulators of inflammatory reactions. Should prostaglandins modulate altered vascular permeability, two possible sites of action are the microvascular bed itself, or adjacent cells which release inflammatory mediators.

Table 1 Effect of Intradermal Injection of Prostaglandin on Inflammatory Lesions Induced by Histamine and Bradykinin

Dose of material (μg)	Response ± s.d. (count in lesion/count in 1 μl blood)	Difference (count in lesion/count in 1 μl blood)	Significance (P) (paired t-test)
Histamine (0.5)	104.4 ± 28.9	—	
Histamine (0.5) + PGE ₁ (1.0)	191.4 ± 11.6	87.0	<0.001
Bradykinin (0.5)	144.2 ± 42.6	—	
Bradykinin (0.5) + PGE ₁ (1.0)	266.7 ± 40.8	122.5	<0.001
PGE ₁ (1.0)	32.9 ± 4.3	—	
Histamine (0.5)	91.1 ± 3.4	—	
Histamine (0.5) + PGE ₂ (1.0)	123.3 ± 20.3	32.2	0.05–0.02
Bradykinin (0.5)	102.9 ± 22.9	—	
Bradykinin (0.5) + PGE ₂ (1.0)	177.8 ± 20.1	74.9	0.02–0.01
PGE ₂ (1.0)	25.4 ± 4.5	—	
Histamine (0.5)	88.1 ± 3.8	—	
Histamine (0.5) + PGA ₁ (1.0)	102.5 ± 15.3	14.4	0.2–0.1
Bradykinin (0.5)	84.1 ± 10.4	—	
Bradykinin (0.5) + PGA ₁ (1.0)	125.9 ± 9.0	41.8	0.01–0.002
PGA ₁ (1.0)	18.6 ± 1.9	—	
Histamine (0.5)	80.5 ± 16.6	—	
Histamine (0.5) + PGF _{2α} (1.0)	68.4 ± 10.5	–12.1	0.5–0.2
Bradykinin (0.5)	88.4 ± 9.6	—	
Bradykinin (0.5) + PGF _{2α} (1.0)	118.0 ± 35.5	29.6	0.01–0.002
PGF _{2α} (1.0)	21.6 ± 3.8	—	
Saline	22.9 ± 6.4	—	
Uninjected skin	12.4 ± 1.0	—	

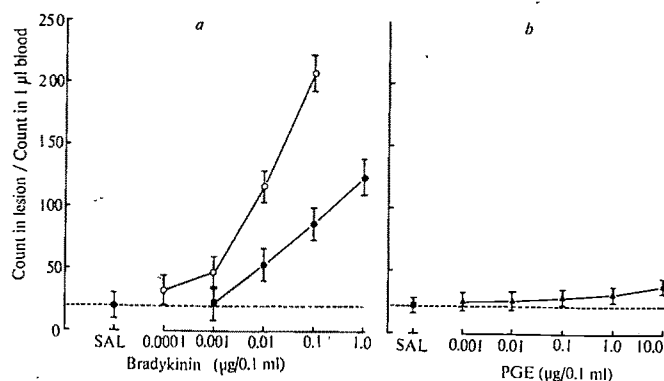


Fig. 1 Dose-response curves in guinea pig skin. Responses represent mean ¹²⁵I-albumin count in lesion/count in 1 μl blood (± 95% confidence limits). *a*, Bradykinin (●); bradykinin mixed with a constant dose (1 μg per 0.1 ml) of PGE₁ (○). *b*, PGE₁ (▲); intradermal saline (0.1 ml) (■).

To ascertain whether prostaglandins act on the vascular bed, their effect on inflammatory lesions induced by intradermal injection of bradykinin and histamine was examined. Inflammatory lesions were evaluated by use of ¹²⁵I-guinea pig serum albumin. Guinea pigs received an intravenous injection of ¹²⁵I-albumin, followed immediately by intradermal injections (0.1 ml) of inflammatory agents using the dorso-lateral skin; doses were allocated to sites according to Latin squares to avoid bias resulting from site and animal variation. After a predetermined time animals were killed and skinned, and disks of skin which included the whole of the lesion were excised with a punch (16 mm diameter) for counting in a well-type γ spectrometer¹⁶. The ¹²⁵I-albumin in 1 μl of blood was also determined for each animal, to provide a reference.

Figure 1a shows the dose-response relationship between extravasated plasma albumin and the dose of intradermal bradykinin over a 30 min period. When PGE₁ (1 μg per dose) was mixed with bradykinin before injection, there was a marked shift of the dose-response curve to the left. The increase in slope of the shifted curve prohibits a potency ratio estimate, but at the level of response to 1 μg

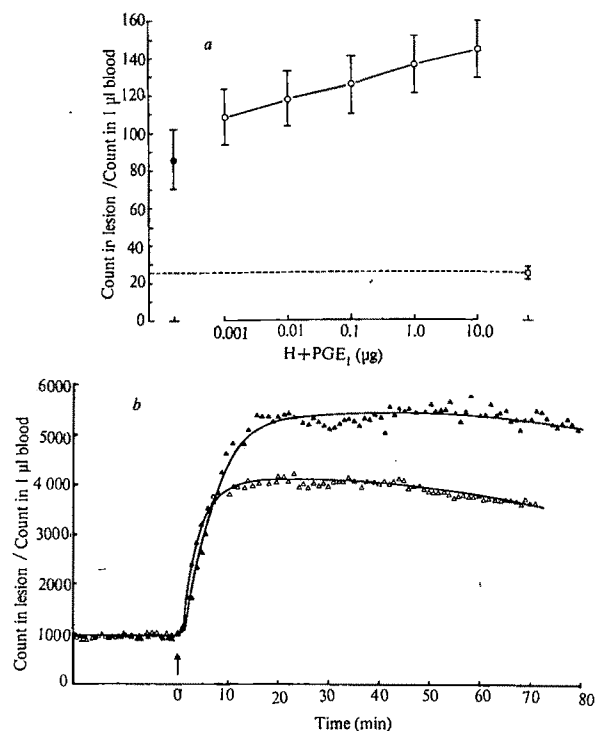


Fig. 2 *a*, H (●), response to intradermal histamine (0.5 μg per 0.1 ml). H+PGE₁ (○), response to histamine (0.5 μg histamine per 0.1 ml) mixed with PGE₁ (doses as shown). □, Uninjected skin. Responses represent mean ¹²⁵I-albumin count in lesion/count in 1 μl blood (±95% confidence limit). *b*, △, Time course of inflammatory response produced by intradermal histamine (2.5 μg histamine per 0.1 ml) at arrow. ▲, Time course of the response to a mixture of histamine (2.5 μg) and PGE₁ (1.0 μg) per 0.1 ml.

of bradykinin the presence of PGE₁ at 1 μg per dose produced a nearly 100-fold increase in the potency of bradykinin. The dose-response relationship of intradermal PGE₁ alone (Fig. 1*b*) shows that the potentiation phenomenon is not simply caused by summation.

Potentiation was also observed when PGE₁ was mixed with histamine before intradermal injection. Potentiation increased with increasing doses of prostaglandin (Fig. 2*a*) and activity was apparent when PGE₁ was present at doses in the order of a few nanograms, indicating a functional significance for the phenomenon.

By a continuous recording technique involving the use of an external γ detector over a single lesion¹⁷, it was shown that potentiation was not accompanied by a substantial prolongation of the response (Fig. 2*b*).

Response potentiation was also observed in varying degrees when histamine or bradykinin was mixed with other prostaglandins (Table 1). In general, potentiation was greater with mixtures of bradykinin and prostaglandin than with mixtures of histamine and prostaglandin (with approximately equipotent doses of agonist). Response potentiation activity ranked PGE₁>PGE₂>PGA₁>PGF_{2α}. The addition of PGF_{2α} to histamine produced a reduction in response but this was not significant by the paired *t*-test, 0.5<*P*<0.2.

We wished to know whether a similar phenomenon might be observed in endogenous inflammatory reactions, where the nature of inflammatory mediators is uncertain and where prostaglandins might act either on the vascular bed itself or on adjacent cells, or at both levels. The effect of local injection of prostaglandins upon three defined allergic inflammatory reactions was therefore examined. Figure 3 shows potentiation by PGE₁ (1 ng–10 μg) of reactions of Type I (passive cutaneous anaphylaxis), Type III (reversed passive Arthus) and Type IV (delayed hypersensitivity) reactions. For Type I reactions, animals received intradermal injections

of skin-fixing antibody 4 h before intravenous injection of antigen, bovine γ-globulin (BGG) and ¹²⁵I-albumin, PGE₁ was injected into skin sites immediately before the intravenous injection and isotope accumulation in the lesion was determined over a 30 min period. For Type III reactions, animals received intradermal injections of antiserum followed 20 min later by an intravenous injection of antigen (BGG) and ¹²⁵I-albumin. PGE₁ was injected into sites immediately before the intravenous injection and isotope accumulation in the lesions determined over a 2 h period. For Type IV reactions, animals were given intradermal purified protein derivative of tuberculin (PPD) 5 weeks after Bacillus Calmette-Guérin (BCG) vaccination. Sixteen hours later animals received intradermal injection of PGE₁ into skin sites, followed immediately by intravenous injection of ¹²⁵I-albumin, isotope accumulation in the lesions being determined over a period of 2 h. Choice of pulse times in these experiments was based upon previous delineation of the time course of these reactions¹⁷.

Prostaglandins E₁, E₂, F_{2α} and A₁ are much less active than histamine or bradykinin at increasing vascular permeability (for example, 10 μg PGE₁ was 1,000–10,000 times less potent than bradykinin). Prostaglandins can, however, cause marked potentiation when injected with histamine and bradykinin, and they are also able to potentiate endogenous inflammatory reactions. In all these situations, potentiating activity could be observed with low concentrations (of the order of a few nanograms) of PGE₁.

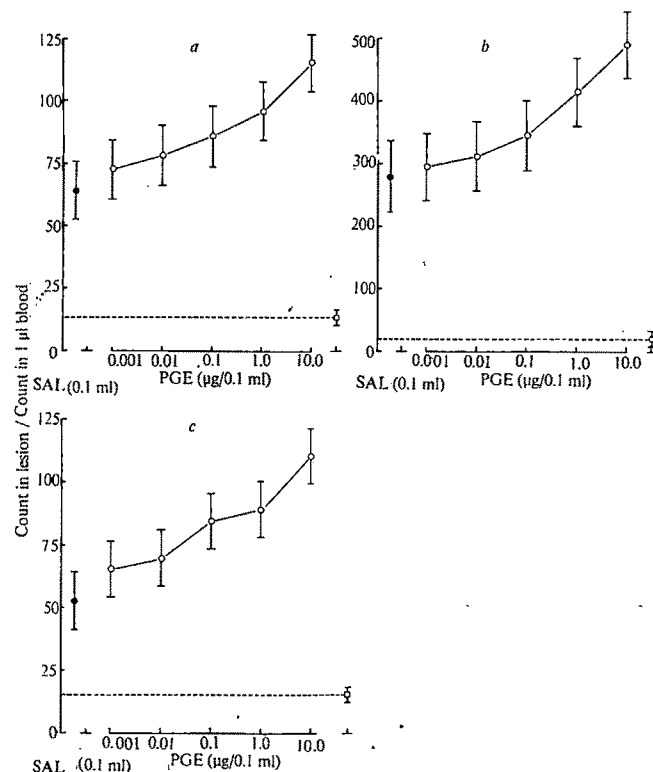


Fig. 3 Effect of a range of doses of PGE₁ on: *a*, Type I reaction (passive cutaneous anaphylaxis); *b*, Type III reaction (reversed passive Arthus); *c*, Type IV reaction (delayed hypersensitivity). ○, Lesions injected with PGE₁ at the doses shown; ●, lesions injected with saline; □, uninjected normal skin. Responses represent mean ¹²⁵I-albumin count in lesion/count in 1 μl blood (±95% confidence limits).

The mechanism of the potentiation of inflammatory exudation induced by prostaglandins remains unestablished. The possibility that their action may depend on local vasodilatation raising the transmural hydrostatic pressure gradient has not been excluded. Parallels with other physiological systems suggest, however, that potentiation may be due either to sensitisation of agonist receptors on vascular endothelial cells,

or to modulation of cyclic AMP levels in endothelial cells through adenylyl cyclase. Similar mechanisms may control the release of mediators from cells adjacent to the vascular endothelium in the case of endogenous inflammatory reactions, involving mediators from mast cells (Type I reactions), polymorphonuclear leukocytes (Type III reactions), or lymphocytes and macrophages (Type IV reactions). In other species (rat and man) prostaglandins have been reported to increase vascular permeability by release of vasoactive amines from mast cells⁷. Clearly, potentiation activity would amplify inflammatory responses produced by release of vasoactive amines, so that the concept of prostaglandins merely acting as intermediates or 'trigger substances' in these species may represent an over-simplification.

We conclude that prostaglandins, by virtue of their activity as modulators of inflammatory responses, may have a major role in inflammatory mechanisms.

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Prostaglandins, Aspirin-like Drugs and the Oedema of Inflammation

OUR discovery that aspirin-like drugs inhibit the biosynthesis of prostaglandins¹⁻³ led to the proposal that this was their main mechanism of action^{1,4}. Several observations have added force to the theory. These include the correlation between relative potencies as prostaglandin synthetase inhibitors *in vitro* and anti-inflammatory activity *in vivo*⁵⁻⁷, the generality of the inhibition in many species and preparations⁸, and the demonstration of release of prostaglandins in inflammation^{9,10} and fever^{11,12}. In addition, prostaglandins of the E series cause an inflammatory response in the skin of rats and man^{13,14} and a fever in cats^{15,16} and man¹⁷.

Prostaglandins cause increased vascular permeability in many species and their potency (on a weight basis) is equal

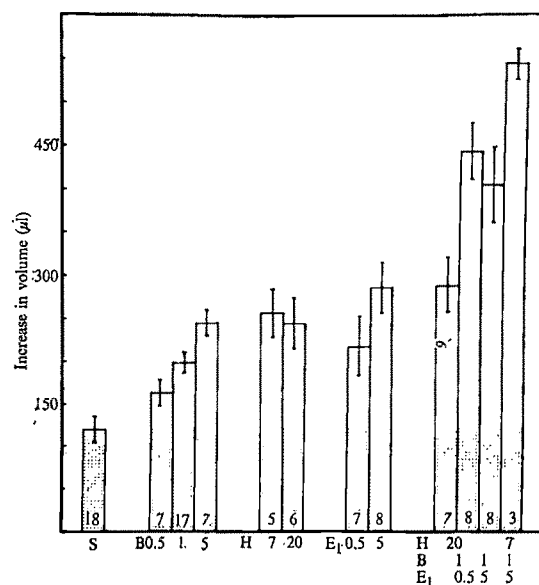


Fig. 1 Potentiation by PGE₁ of the rat paw swelling induced by bradykinin or histamine. The bars show the mean ($\pm$ s.e.m.) increase in paw volume (μ l) 30 min after injection of 0.1 ml saline (S), bradykinin (B), histamine (H), PGE₁ or mixtures as specified. The effects of saline alone are shaded across the figure to allow easier comparison of the added effects of the other substances. Numbers inside the bars refer to numbers of paws used. Note that addition of PGE₁ either to histamine or to bradykinin substantially increased the paw swelling, but addition of bradykinin to histamine did not.

to that of bradykinin and somewhat higher than that of 5-hydroxytryptamine (serotonin) and histamine¹⁸. The oedema induced by prostaglandins is not, however, dose-dependent as it is with bradykinin; indeed higher doses of prostaglandin E₁ (PGE₁) inhibit the oedema caused by other mediators¹⁹. Additive effects, rather than synergism, were also demonstrated between prostaglandins and histamine, bradykinin or carrageenin injections¹⁹.

We have shown that PGE₁ and PGE₂ sensitise the pain receptors to mechanical and chemical stimulation and suggested that the analgesic action of aspirin-like drugs could be explained by the abolition of the sensitisation caused by the local release of prostaglandins during an inflammatory reaction²⁰⁻²². The present experiments were designed to test whether a similar mechanism could account for the pro-inflammatory actions of prostaglandins. We have reinvestigated the interaction between prostaglandins and other putative mediators and carrageenin-induced oedema. Wistar rats of either sex weighing 150-250 g were used. In the first series of experiments, injections (0.1 ml) of different substances were given into the plantar region of the hind paws. Substances used included PGE₁ (0.5-5 μ g), bradykinin (1-5 μ g) and histamine (7-20 μ g); they were given either alone or in mixtures as specified later.

In the second series of experiments, carrageenin (2% w/v in saline) was injected into the hind paws to induce inflammation. All but the control animals were treated with indomethacin (20 mg kg⁻¹, 30 min beforehand in Tris buffer at pH 8). In the indomethacin-treated group, some rats received a mixture of carrageenin and either PGE₁ (0.1-0.5 μ g), PGE₂ (0.1-0.5 μ g), PGF_{2 α} (0.5 μ g), bradykinin (1 μ g) or histamine (20 μ g).

Injections were made into both hind paws in random order; the oedema was measured by the mercury displacement method²³.

Figure 1 summarises the results obtained by injecting inflammatory mediators into the rat paws. To facilitate comparison of the effects of the mediators, above the increased paw volume caused by saline alone, the saline effect has been shaded on the figure. There was a dose-dependent effect of

bradykinin but no significant increment ($P > 0.5$) to varying concentrations of histamine or PGE_1 . These results agree with those of Glenn¹⁹.

The histamine-bradykinin mixture produced an effect no greater than that of histamine alone. The effects caused by mixtures containing PGE_1 were, however, substantially greater for histamine and for bradykinin than those expected by simple addition. Increasing the dose of PGE_1 from 0.5 to 5 μg did not increase the potentiating activity.

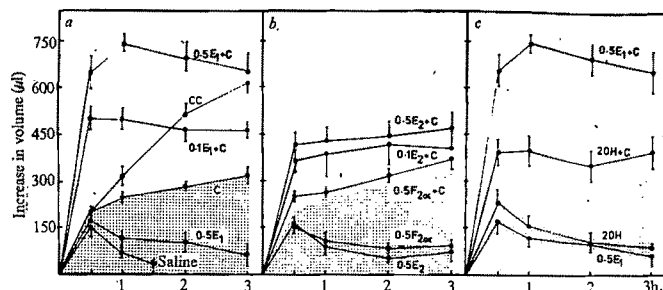


Fig. 2 Potentiation by PGE_1 or PGE_2 of the rat paw swelling induced by carrageenin in the presence of indomethacin. Panel *a* shows the effects of carrageenin alone (CC) over a 3 h period. To facilitate comparison, the swelling induced by carrageenin in the presence of indomethacin (C) is shown as a shaded area in each panel. Prostaglandin E_1 (0.1 μg ; 0.1 $\text{E}_1 + \text{C}$) substantially increased the paw swelling induced by carrageenin, and 0.5 μg (0.5 $\text{E}_1 + \text{C}$) was even more effective. Panel *b* shows similar but smaller effects for PGE_2 but no effect with $\text{PGF}_{2\alpha}$. Panel *c* shows that 20 μg histamine (20 H + C) had a potentiating effect similar to that of 0.1 μg PGE_1 . Curves inside shaded areas in the three panels show the effects of PGE_1 (0.5 μg), PGE_2 (0.5 μg), $\text{PGF}_{2\alpha}$ (0.5 μg), histamine (20 μg), or saline (0.1 ml) given alone.

Figure 2 shows the effects of addition of various substances on the paw swelling induced by carrageenin. Panel *a* shows that indomethacin reduced the paw swelling induced by carrageenin alone. In order to test the effects of exogenous prostaglandins on the paw swelling induced by carrageenin, it was necessary to suppress endogenous prostaglandin formation by pretreatment of the rats with indomethacin. In these animals, PGE_1 , PGE_2 or $\text{PGF}_{2\alpha}$ (0.5 μg ; 5, 4 and 4 experiments respectively) caused no greater paw swelling at 30 min than did saline alone (8 experiments), but their effects lasted for a longer time. There was little or no difference between the paw swelling induced by the three prostaglandins at this dosage, but their effects on the oedema produced by carrageenin in the presence of indomethacin (shown as a shaded area on the graphs) varied substantially. Prostaglandin E_1 (0.1 μg , 5 experiments) potentiated the paw swelling at 30 min and at 0.5 μg (6 experiments) the effect was even greater. Prostaglandin E_2 (0.1 μg , 6 experiments; 0.5 μg , 9 experiments) was about one-fifth as potent as PGE_1 and $\text{PGF}_{2\alpha}$ (0.5 μg , 8 experiments) gave no potentiation. At the time (30–60 min) when the PGE_1 and PGE_2 were producing maximal potentiation of the carrageenin paw swelling they had no greater effect than saline when given by themselves. Histamine (20 μg , 8 experiments) gave some augmentation of the paw swelling induced by carrageenin in the presence of indomethacin but the effects were less than, or equal to, the potentiating action of PGE_1 at 0.1 μg , that is, it was at least 200 times weaker than PGE_1 . Bradykinin (1 μg , 5 experiments) had no potentiating effect on the carrageenin paw swelling.

These experiments support our hypothesis that prostaglandins E_1 and E_2 potentiate the oedema-producing capacity of other inflammatory mediators. Assay of mediators in inflammatory exudate produced by carrageenin in the rat showed release of both histamine and bradykinin in the early phase but that of PGE_2 only after two to three hours⁹. Thereafter the concentrations of $\text{PGF}_{2\alpha}$ and histamine increased

steadily and paralleled the time course of migration of polymorphonucleocytes into the site of injury²⁴. Our results, which show that indomethacin has an inhibitory effect on the carrageenin-induced oedema as early as 1 h after injection, are in agreement with those of other authors²⁵ and suggest that at the time when there is little or no migration of polymorphonucleocytes there is already a release of prostaglandin by the local cells and that this release potentiates the effects of the other mediators. Phagocytosis by polymorphonucleocytes also releases prostaglandins²⁶, so there could be a contribution to the potentiation from this source also. We propose therefore that the role of prostaglandins in the oedema of inflammation is to intensify the effects of the other chemical mediators. In this respect, their activity parallels that which we found for the pain of inflammation^{20–22}. Such an action explains why aspirin-like drugs only reduce but do not abolish the response to an inflammatory stimulus. For example, in this work and previously^{24,25,27}, the rat paw swelling induced by carrageenin was reduced by less than 60% by high doses of anti-inflammatory substances such as indomethacin.

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Incorporation of Rhodopsin Proteolipid into Bilayer Membranes

RHODOPSIN constitutes over 80% of the membrane-bound protein in the outer segment of rod photoreceptors^{1,2}. Absorption of light by rhodopsin leads to large changes in the ionic current of the receptor cell³: excitation of a single rhodopsin molecule transiently (~ 1 s) stops about 10^7 Na ions from flowing across the plasma membrane of the outer segment^{4,5}. The mechanism by which the excited rhodopsin molecule achieves such large reduction in ionic flux is not understood, partly because natural rhodopsin-containing membranes amenable to the experimental methods required to investigate the transport properties of rhodopsin have not been successfully prepared. As an alternative to natural membranes, attempts to form model membranes which incorporate the properties of the photoreceptor have been made. Takagi *et al.*⁶ and Fesenko *et al.*⁷ have reported the incorporation of ultrasonicated fragments of rod outer segments into model membranes. In this study we report the successful incorporation of native, purified rhodopsin into bilayer membranes. This should make possible the investigation of the mechanism by which rhodopsin molecules act in the rod photoreceptor.

Two recent advances have permitted us to incorporate rhodopsin into model membranes. One is the report by Hong and Hubbell⁸ on the preparation of detergent-free phospholipid vesicles containing purified rhodopsin. The other is the report by Montal and Mueller⁹ on the formation of lipid bilayers, in the absence of any organic solvent, by the hydrophobic apposition of lipid monolayers. In the method of Montal and Mueller monolayers of lipids dissolved in a readily volatile solvent are spread on an air-water interface in each of two compartments. The compartments are separated by a hydrophobic partition in which there is a small (about 0.25 mm diameter) aperture. After the solvent evaporates, a bilayer is formed by raising the water level in two compartments above the level of the aperture. The hydrocarbon tails of the lipids in the two monolayers oppose each other across the aperture forming the bilayer. To incorporate rhodopsin into these model membranes, therefore, it was first necessary to form lipid monolayers containing native, purified rhodopsin.

To extract rhodopsin, rod outer segments from dark-adapted bovine retinas (Hormel Co.) were isolated by sucrose flotation, and purified in a discontinuous sucrose gradient¹⁰. Phospholipid vesicles containing rhodopsin were prepared following the method of Hong and Hubbell⁸. Dodecyl trimethyl ammonium bromide (DTAB) (Eastman Co.) (100 mM) which had been recrystallised twice was used to extract rhodopsin. Phospholipid recombinants were made with chromatographically pure egg lecithin (General Biochemicals). Recombinants were made with three different molar ratios of lecithin to rhodopsin: 100:1, 50:1, and 25:1 assuming an extinction coefficient for rhodopsin of 40,600 at 498 nm (ref. 11). Unlike Hong and Hubbell we did not delipidate the rhodopsin-DTAB micelles before recombination with the phospholipid, so the total phospholipid to rhodopsin mol ratio must be larger than what we report here. The detergent was removed by exhaustive dialysis (4 d in the dark at 4° C) against 5 mM Tricine (Tris(hydroxymethyl)methyl glycine), pH 7.0. At the end of

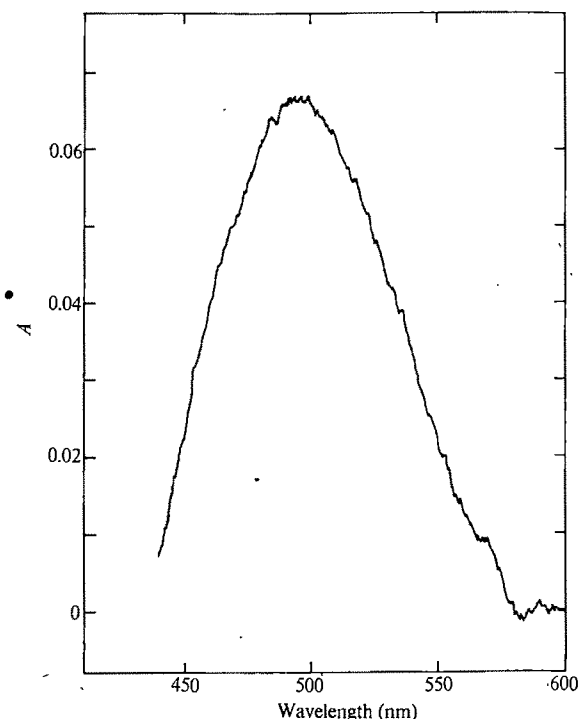


Fig. 1 Difference spectrum of rhodopsin in hexane. The absorption spectrum was measured in a Cary 14 spectrophotometer with the use of a 1 cm path length cuvette in a temperature-regulated jacket (10° C). The spectrum shows a peak with $\lambda_{\max}$ at 498 nm.

the dialysis period the water-soluble rhodopsin lipoprotein vesicles were collected by centrifugation.

To form monolayers, the water-soluble rhodopsin lipoprotein must be extracted into an organic solvent and must not be denatured. In this study we attempted to extract rhodopsin lipoprotein into hexane by charge neutralisation with Ca, since it might be expected that ion-pair formation between Ca and the hydrophilic groups in the lipoprotein would enhance the solubility of the lipoprotein in solvents of low dielectric constant¹². Rhodopsin lipoprotein was dispersed in 4 ml of distilled water in a tube at concentrations of 0.25 and 0.5 mg ml⁻¹. One ml of hexane and 0.2 ml of a 100 mM CaCl₂ solution were added to the dispersion in rapid succession. The tube was vigorously mixed for 5 min and the two immiscible phases were then allowed to separate. Within 30 min more than 90% of the protein was extracted from the aqueous phase into the non-aqueous phase. Within 6 h the aqueous phase was completely clear indicating total lipid extraction. Extractions were routinely carried out in the dark at 4° C. Control experiments indicated, however, that extraction at room temperature was equally successful. After extraction the hexane phase had a characteristic red colour, was turbid and changed to a distinct yellow colour following illumination.

Absorption spectra in the visible range of the organic solvent phase showed a peak with $\lambda_{\max}$ at 498 nm (Fig. 1) which disappeared upon illumination. This result indicates that we succeeded in extracting native rhodopsin lipoprotein into hexane by ion-pair formation with Ca. We have thus formed a rhodopsin proteolipid, that is, a complex of lipid and protein which shares solubility properties with lipids¹³. Extraction of native rhodopsin was also successful with other organic solvents such as pentane and ether. Attempts to regenerate bleached rhodopsin in the organic solvent by addition of 11-*cis* retinal have failed so far.

In agreement with previously reported data on the extraction of cytochrome c into organic solvents¹⁴, we found that divalent cations (Ca, Mg) were more effective than monovalent cations (Na, K) in extracting rhodopsin into hexane.

and that Ca was more effective than Mg. The turbidity of the organic phase suggests that some water must have been extracted into hexane along with protein and lipid. We have not quantified the extent of water extraction. It is, however, expected that some water could have been extracted since rhodopsin is partially hydrophilic, as suggested by its amino acid composition¹⁵, the presence of carbohydrate residues covalently attached to it^{16,17}, and X-ray scattering data which indicate that rhodopsin in the photoreceptor membrane is partially surrounded by water¹⁸.

The rhodopsin proteolipid in hexane spreads into a monolayer when placed at an air-water interface. These monolayers could be used to form rhodopsin-containing bilayers following the method of Montal and Mueller. Monolayers were spread on a clean aqueous solution surface as condensed films at their own lens pressure. Bilayers were formed upon raising the solution level on both sides of the hydrophobic partition by injecting solution into the two compartments with syringes. We attempted at first to form symmetrical membranes by apposing two monolayers containing rhodopsin proteolipid. The membranes formed under these conditions were, however, extremely unstable. To increase stability we formed asymmetric membranes simply by apposing monolayers of different chemical composition¹⁹. One monolayer was formed with a mixture of glycerol dioleate (Arma Chemicals) and cholesterol (Sigma) dissolved in hexane, while the other was formed with the rhodopsin proteolipid.

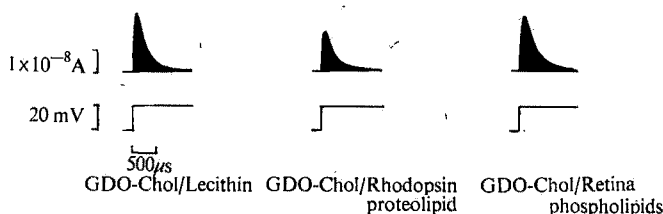


Fig. 2 Membrane current in response to 20 mV voltage pulses across asymmetric bilayers. The upper trace in each record is current and the lower trace is voltage. Voltage pulses were repeatedly applied (5 per s) and the current traces were superposed on a storage oscilloscope. Asymmetric membranes were formed by apposition of two monolayers of different chemical composition. The records presented correspond to three different membranes. In all three membranes one monolayer was formed with a mixture of glycerol dioleate-cholesterol (1:0.26 molar ratio) dissolved in hexane, while the other monolayer was formed with either egg lecithin in hexane, or rhodopsin proteolipid in hexane or phospholipids extracted from bovine retinae (6 mg ml⁻¹) with chloroform:methanol (2:1 v/v) and purified in a silicic acid column. Rhodopsin-containing monolayers were formed with proteolipid extracted for at least 6 h from a 0.25 mg protein ml⁻¹ dispersion in water of either 50:1 or 25:1 lecithin:rhodopsin recombinants. All monolayers were spread over a 5 mM aqueous solution of Tricine, pH 7.0. All membranes were formed across the same aperture (6 × 10⁻⁴ cm²). The membrane capacitance measured by integration of the current records illustrated is: GDO-Chol/lecithin, 1.05 μF cm⁻²; GDO-Chol/rhodopsin proteolipid, 0.67 μF cm⁻²; GDO-Chol/retina phospholipids, 1.0 μF cm⁻².

The electrical properties of the membranes were studied under conditions of voltage clamp. Constant voltage pulses were repeatedly applied across the membrane, and the membrane current in response to these pulses was recorded. Membrane capacitance was determined by integration of the membrane current records according to the formula:

$$C = \frac{\int i dt}{V}$$

where C is membrane capacitance, i is membrane current and V is the magnitude of the applied voltage step. In Fig. 2 we present typical records. Analysis of these and other records is shown in Table 1. Asymmetric lipid bilayers made

with glycerol dioleate-cholesterol on one side and egg lecithin or phospholipids extracted from bovine retinas on the other side are indistinguishable from each other. They both have a capacitance of about 1 μF cm⁻² and a resistance of 10⁸–10⁹ Ω cm². These values are typical of membranes made with a variety of lipids in the absence of any organic solvent. In contrast, membranes made with glycerol dioleate-cholesterol on one side and rhodopsin proteolipid on the other have a distinctly smaller capacitance of only about 0.65 μF cm⁻². In the dark, the resistance of the rhodopsin-containing membrane is comparable to that of the unmodified membrane: 10⁸–10⁹ Ω cm². Thus, incorporation of rhodopsin in the dark does not affect membrane resistance, but does reduce membrane capacitance.

Table 1 Capacitance of Asymmetric Bilayer Membranes

Composition	Capacitance (μF cm ⁻²)	Dielectric thickness (Å) ‡
GDO-Chol*/lecithin	1.0 ± 0.1 (8) †	19
GDO-Chol/retina phospholipids	1.0 ± 0.1 (8) †	19
GDO-Chol/rhodopsin proteolipid	0.65 ± 0.08 (8)	29

* Glycerol dioleate: cholesterol (1:0.26 molar ratio).

† Average ± s.d. (number of measurements).

‡ Assuming ε = 2.1 (hexadecane) inside the membrane.

The change in membrane capacitance on incorporation of rhodopsin can arise from changes in dielectric constant, dielectric thickness or both. Careful measurement of the dielectric constant of both the unmodified and the rhodopsin-containing membranes is needed before a complete explanation can be given for the change in membrane capacitance. It is clear, however, that incorporation of a partially hydrophilic protein into a membrane would, if anything, increase the dielectric constant thus increasing the membrane capacitance with respect to that of an unmodified membrane²⁰. Therefore, if we assume that the dielectric constant does not change upon incorporation of rhodopsin, we can calculate a lower boundary for the effective dielectric thickness of the rhodopsin-containing membrane using the expression:

$$l = \epsilon A / 4\pi C$$

where C is membrane capacitance, A is area, ϵ is the dielectric constant and l is the effective dielectric thickness. Estimating 2.1, the dielectric constant of a long chained hydrocarbon, to be the dielectric constant of both the modified and the unmodified membranes, the dielectric thickness of a lipid membrane is 19 Å and the dielectric thickness of the rhodopsin-containing membrane can be no smaller than 29 Å. The hydrocarbon region of the rhodopsin-containing membrane in rods is 28 Å thick^{21,22}. The rapid rotational motion of rhodopsin in the photoreceptor membrane has led Cone²³ to propose that rhodopsin might act as a light-activated diffusional carrier which transports Ca ions by tumbling across the hydrophobic region of the membrane. The fact that the hydrocarbon region of the rhodopsin-containing membrane is thin suggests an alternative mode of action for rhodopsin as a diffusional carrier which does not require the thermodynamically improbable tumbling of a partially hydrophilic glycoprotein into a hydrophobic phase. If excitation of rhodopsin exposes Ca binding sites which are not available in the dark, then the charge neutralisation which might result from ion-pair formation with Ca would allow rhodopsin to sink deeper into the hydrocarbon region of the membrane, much in the way that Ca permits extraction of rhodopsin into hexane as reported here. In the thin hydrocarbon region of the photoreceptor membrane (~28 Å) the large (~45 Å diameter²⁴) rhodopsin molecule need only sink a few Å to cross the low dielectric region. Thus, rhodopsin might translocate Ca ions across the membrane not by

tumbling, but rather by bobbing in the membrane. Indeed, Blasie¹⁸ has interpreted the changes in X-ray scattering by the photoreceptor membrane that follow illumination as resulting from rhodopsin molecules sinking by about 10 Å into the hydrophobic region of the membrane.

The rhodopsin-containing model membranes have so far been short-lived, with an average lifetime of only about 1 min, making the search for light effects difficult. We have, however, investigated the effects of bright flash illumination on the capacitance of these membranes, and have not distinguished any effects within the resolution of our method. Future investigation will pursue the effects of light on the transport properties of rhodopsin in these model membranes.

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Fate of Bacteriophage Lambda in Non-immune Germ-free Mice

THE clearance of colloidal particles in animals has been studied in several experiments¹⁻¹⁰. The use of bacteriophage in such studies offers a sensitive tool to augment materials such as dyes, radioactive colloids and enzymes for analysing mechanisms of handling foreign particulate material. Furthermore, such use of bacterial viruses may enhance the general under-

Studies of the intracellular distribution of phages ϕ X174 and T2 in the organs of rabbits and guinea pigs demonstrated that when they were taken up by the cells of the reticuloendothelial system (RES), most plaque-forming units (PFU) became localised in the larger granular fraction (lysosomes and mitochondria) of the cells². Inchley *et al.* studied the response of mouse macrophages to injected phage T4^{11,15,17}, finding that within 30 min of ¹²⁵I-T4 injection, more than 99% of the phage was phagocytosed by liver Kupffer cells. Inchley also found that T4 PFU could be recovered from the spleen 5 d after the initial injection¹¹. Extensive studies have shown that elimination of colloidal particles is exponential with time regardless of whether these particles were phage^{11,15,17}, animal viruses¹⁸ or inert substances^{1,19}.

Our studies of the fate of phage λ , injected by several routes into NIH germ-free mice, differ from previous studies in several ways. First, previous investigations focused on elimination of foreign particles, either by phagocytosis or by antibody formation, while we were interested in the distribution of phage which survive rapid elimination. Second, most studies have used isotopic label to determine the location of the injected particles without showing whether the particles retained their biological activity, while we assayed for the ability to make plaques. Third, previous investigations concerned tissues known to be involved in the RES, while we were interested in any tissue accumulating phage. Fourth, our phage could be distinguished from possible contaminants by its genetic markers (Table 1). Fifth, the use of germ-free animals precluded interactions with microorganisms in the gastrointestinal tract, although the germ-free mouse system is not an ideally "clean" system for experimental purposes, for leukaemia viruses and other virus-like particles have been found in the thymus glands of such mice²¹⁻²⁴.

Table 1 Pattern of Test Results by which λ pgal₈₅₇CI857 (ref. 20) can be distinguished from Possible Contaminating Phage

Phage	Plaques on pm+ host	Plaques on pm- host	Plaques at 34° C	Plaques at 40° C	Plaques on λ lysogen	Red plaques on MacConkey's gal with gal- host
λ pgal ₈₅₇ CI857	+	-	Turbid	Clear	-	+
Wild type λ	+	+	Turbid	Turbid	-	-
Wild type or virulent phage	+	+	Clear	Clear	+	-

The phage were checked periodically for their ability to transduce the galactose operon, for the presence of CI857 (production of a heat-sensitive repressor) as manifested by clear plaques at 40° C and turbid plaques at 34° C, and for sensitivity to λ immunity as demonstrated by the inability of the phage to plate on a *su*₁₁₁⁺ λ lysogen.

Figure 1 shows that the gross distribution of the virus was tissue-specific, regardless of the injection route. This, however, was not true with force-feeding, which failed to introduce significant amounts of virus to any tissues and spaces examined. Little, if any, virus was detected in the faeces after injection intraperitoneally, intramuscularly, intravenously or *per os*.

By 3 h after infection the blood contained considerably more virus than the peritoneal fluid even if the virus were given intraperitoneally. Within 48 h the virus was cleared from the blood (<10 PFU ml⁻¹) and the peritoneum, no matter where the virus was introduced.

All the organs examined in the infected animals contained viable phage. Of these organs, the spleen had the highest titre. With increasing time, the titre of phage within the liver decreased rapidly. The results were similar with the thymus. Within 3 h after intraperitoneal, intramuscular, and intravenous administration of virus the titre of virus in the spleen in PFU g⁻¹ of

after infection, the blood titre had decreased to zero while the spleen titre still exceeded 10^4 PFU. This difference between the spleen and other organs increased with time.

The titres of phage found in any of the organs and in the two body spaces analysed were higher if the phage were injected intraperitoneally. This might indicate that the phage within the

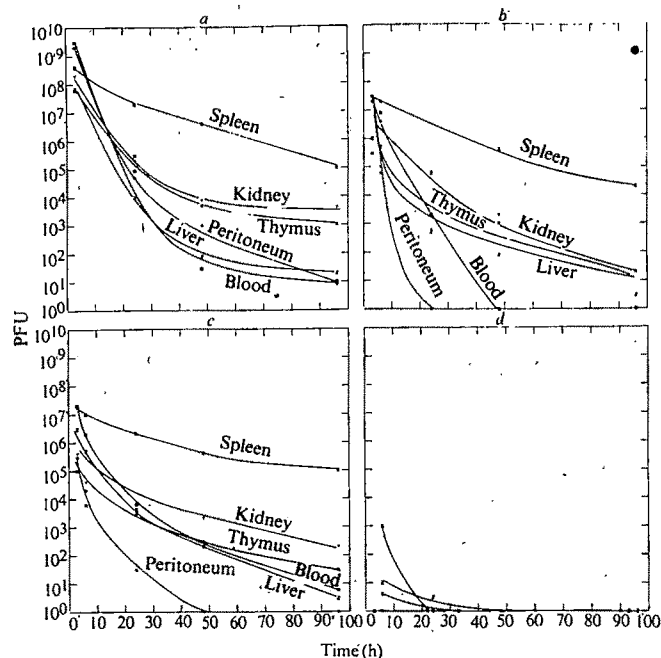


Fig. 1 Plot of the number of PFU g^{-1} wet tissue detected in: blood ($\odot$); peritoneum ($\diamond$); spleen ($\times$); liver ($\square$); thymus ($\otimes$); and kidney (γ); as a function of time after injection of phage by several routes: intraperitoneal (a); intramuscular (b); intravenous (c), and per os (d). λ *pgal*₈₅, CI857, grown vegetatively on *E. coli* C600 (ref. 25), was purified using a CsCl gradient²⁶. NIH albino germ-free mice of mixed sexes were maintained in a plastic Trexler-type isolator unit provided by the Laboratory Aids Branch at NIH²⁷⁻³⁰. Sterility checks were made by streaking samples of organs, faeces, urine and blood onto Tryptone B1 plates to demonstrate the absence of bacteria and by titrating the samples against several strains of *E. coli* to demonstrate the absence of coliphage. All experiments with the germ-free animals were done within the isolator, and not with animals removed from the gnotobiotic environment. All materials passed into the isolator through an air-lock were either autoclaved for 20 min at 121°C, or swabbed with peracetic acid. The acid destroyed the coliphage used in these experiments. 2×10^{12} PFU of *E. coli* phage λ *pgal*₈₅, CI857 were injected intramuscularly, intravenously, intraperitoneally or per os. Phage samples in 0.2 ml phosphate-buffered saline (PBS) containing 0.01 M $MgSO_4$ were injected intravenously into the tail vein or intramuscularly into the quadriceps femoris muscle group. The intraperitoneal injections of phage in 0.5 ml PBS were given in the right middle quadrant, caudal to the liver. A mouse restrainer (Fisher) was used to facilitate injection procedures. A polyethylene tube 0.03 inch in diameter, forced down the oesophagus, was used to force-feed the phage sample in 0.2 ml PBS. At 3, 6, 24, 48 and 96 h after injection, mice from each injection group were anaesthetised with ether, the common carotids and jugular veins were cut and the blood was collected in a small test tube. The animals were pinned to a wooden board within the isolator and 3 ml of PBS was injected into the peritoneal cavity. After 1-2 min, the cavity was physically massaged and 0.5-1.5 ml of fluid was withdrawn. Faecal samples were collected when available. The animals were then dissected to remove the spleen, one kidney, the left lobe of the liver and (usually) the left lobe of the thymus. Each of the organs was washed thoroughly with PBS, and final washings were saved and titred to demonstrate that there was little or no phage remaining on the surface of the organs. This indicated that the virus was firmly associated with the organ samples and was not virus from the peritoneal fluid that had coated the organ. All samples were passed out of the isolator for further analysis. A 0.5 ml sample of PBS was added to each organ which was then ground with a sterile sintered glass pestle. Faecal samples were treated in the same way. The samples were titred against DB1 using an agar overlay method³¹. The presence of con-

peritoneal cavity were taken up preferentially by the liver and then the spleen, whereas phage injected intramuscularly or intravenously were distributed more uniformly. This agrees with earlier findings³² that compounds administered intraperitoneally are taken up by the portal circulation. Thus the liver maintains the highest concentration of injected substances. Particles injected intramuscularly and subcutaneously were distributed by the heart; because 28% of the cardiac output reaches the liver, the liver should have theoretically fewer particles within its substance when injected by other than the intraperitoneal route. Our results were similar. Therefore the effects, the metabolism and the excretion of phage might be different when injected by varied routes, for varying percentages of injected phage came into contact with the liver.

The spleen retained high titres of injected intact phage (10^5) for prolonged periods of up to 7 d. Inchley also found intact phage in the spleen up to 5 d after infection³³.

Retention of phage in the spleen was previously suggested to be due to the fact that "inactivation of antigen occurs much more rapidly within Kupffer cells than within splenic macrophages"³⁴. This interpretation predicted that the spleen, well-endowed with macrophages, would retain lower titres of phage than other tissues deficient in macrophages, such as the kidney. Our data (Fig. 1) suggested an alternative interpretation that the spleen was engaged in non-destructive capture of antigens. The spleen can carry out phagocytosis, but recently a non-phagocytic capturing method utilizing the Schweigger-Seidel capillary sheaths was described³⁵. This latter mechanism might be responsible for the non-destructive capture of phage that we observed. This ability to non-destructively retain antigen might allow the spleen to serve as a continued source of antigen for the stimulation of antibody formation.

Although it was suggested that non-phagocytic antigen capture by the Schweigger-Seidel reticulum cells required interaction with antibody³⁶, in our experiments such an interaction was remote, for we were unable to detect neutralising antibody to λ ($K < 10^{-3}$)³¹.

Antigen trapping in the spleen may be closely coupled to antibody formation. An intact spleen is necessary for maximal antibody response³⁷. The removal of the spleen severely depresses the antibody response in mice, and this defect in antibody formation following splenectomy cannot be corrected by injection of splenic elements³⁷. Furthermore, in neonatal rats and mice the spleen is an alymphoid organ^{3,4}. The ability to trap antigen appears 2 weeks after birth^{3,4}. Multiple injections of antigen are required during this first 2-week period to stimulate antibody formation, whereas no single injection during this time produces an antibody response⁴. Following the development of the lymphoid elements in the spleen a single injection of antigen stimulates formation of antibodies. These observations indicate that the structural integrity of the spleen might allow cell-to-antigen and cell-to-cell interaction for antibody formation^{2,5,8,19-25,34-39}.

The rapid elimination of phage in intact animals may explain the limited success of phage treatment of infectious diseases⁴⁰ and may interfere with attempts to observe prokaryotic viral gene expression^{41,42} in whole animals. This rapid rate of elimination may be slowed by overwhelming the RES with inert colloidal particles such as Thorotrast (thorium dioxide)^{19,43}.

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osmotica in the ratio of 1:4 to give the final concentrations of enzymes shown in Table 1, and incubated at 28° C in the dark.

The arrangement of microspores in a few tetrads of *D. metel* (about 5%) was isobilateral but the predominant organisation was tetrahedral. Initially, the four microspores within the massive enveloping wall of the tetrad (Fig. 1a) were naked, but they subsequently developed thin cellulose walls, at which stage they could easily be released from the envelope by gentle pressure. Conventional methods were then used to obtain free protoplasts. The cell walls of both immature and mature pollen grains were resistant to the enzymes used in this study. The mature pollen grains germinated readily and the pollen tubes were then susceptible to enzyme action. Their contents, however, were released as sub-protoplast fragments and not as entities.

Table 1 Effect of Enzyme-Osmotica on Release of Protoplasts from Pollen Tetrads of *Datura metel**

No.	Treatment †	Period of incubation (h)		
		1	4	6
1	CSS	—	++	+++
2	CR	—	+	++
3	CA	—†	++	+++
4	H	—	—	—
5	P	—	—	—
6	SDJ	+	+++	+++
7	CSS+H	—†	++	+++
8	CR+H	—	+	++
9	CA+H	—	++	+++
10	CSS+P	—†	++	+++
11	CR+P	—	+	++
12	CA+P	—†	++	++
13	CSS+SDJ	++	+++	++++
14	CR+SDJ	+	++	+++
15	CA+SDJ	++	+++	++++
16	H+P	—	—	—
17	H+SDJ	+	+++	+++
18	P+SDJ	+	+++	+++
19	CSS+H+SDJ	++	+++	++++
20	CR+H+SDJ	+	+++	+++
21	CA+H+SDJ	++	+++	++++
22	CSS+P+SDJ	++	+++	++++
23	CR+P+SDJ	+	++	+++
24	CA+P+SDJ	++	+++	++++

* Percentage yield; —, 0; +, <20; ++, 20–50; +++, 51–80; and +++, >80. † CSS, Cellulase Onozuka SS (from *Trichoderma viride*), all Japan Biochemicals, 5%; CR, Cellulase Type III (from *Rhizopus* mould), Sigma, 10%; CA, Cellulase Type II (from *Aspergillus niger*), Sigma, 10%; H, Hemicellulase grade II (from *Rhizopus* mould), Sigma, 5%; P, Pectinase, Nutrition Biochemicals, 5% (all concentrations as w/v); and SDJ, snail digestive juice (from *Helix pomatia*), Koch-Light, 2% (v/v). ‡ Occasionally, 1 to 2% of tetrads released their protoplasts.

Nuclear Divisions in Protoplasts isolated from Pollen Tetrads of *Datura metel*

THE significance of haploid protoplast research has been discussed by Bhojwani and Cocking¹. They have succeeded in isolating protoplasts from microspores and bringing about regeneration of cell walls. The occurrence of nuclear divisions in protoplasts isolated from pollen tetrads of *Datura metel* L., a plant in which androgenesis could be experimentally induced^{2,3}, is described here.

Anthers from several buds were pooled in three groups, each of which contained either pollen tetrads, immature microspores or mature pollen grains. Segments of about 5 mm were excised from the central region of anthers and their contents gently squeezed out into 10% sucrose solution. The suspension volume for each group containing an entirely homogeneous cell population was adjusted to about 25×10^4 cells ml⁻¹. Enzymes were prepared as stock solutions in 0.05 M potassium acetate buffer, pH 5.4, containing 10% sucrose. The cell suspensions were mixed with the enzymes

Protoplasts from pollen tetrads were isolated in twenty-one of twenty-four enzyme-osmotica tested. Mixtures containing a cellulase (irrespective of its origin) or snail digestive juice (helicase) were effective, but pectinase and hemicellulase were ineffective (Table 1). The release of protoplasts in osmotica containing only cellulase (used as controls) was unexpected and contrary to earlier findings¹. This could not have resulted if callose (which is resistant to cellulase) were the only constituent of the tetrad wall. The snail enzyme complex which contains β -1,3- and β -1,4-glucan glucanohydrolases that degrade callose and cellulose, respectively, was comparable in its action with that of cellulase. Cellulase in conjunction with helicase, however, accelerated the rate at which protoplasts were released. The final yield was also higher. Similar observations have been recorded for *Atropa belladonna*, *Lycopersicon esculentum* and *Solanum xanthocarpum* (unpublished data). These findings suggested that the tetrad walls of *D. metel*, and possibly those of the others, contained cellulose in addition to callose. Lysis of either

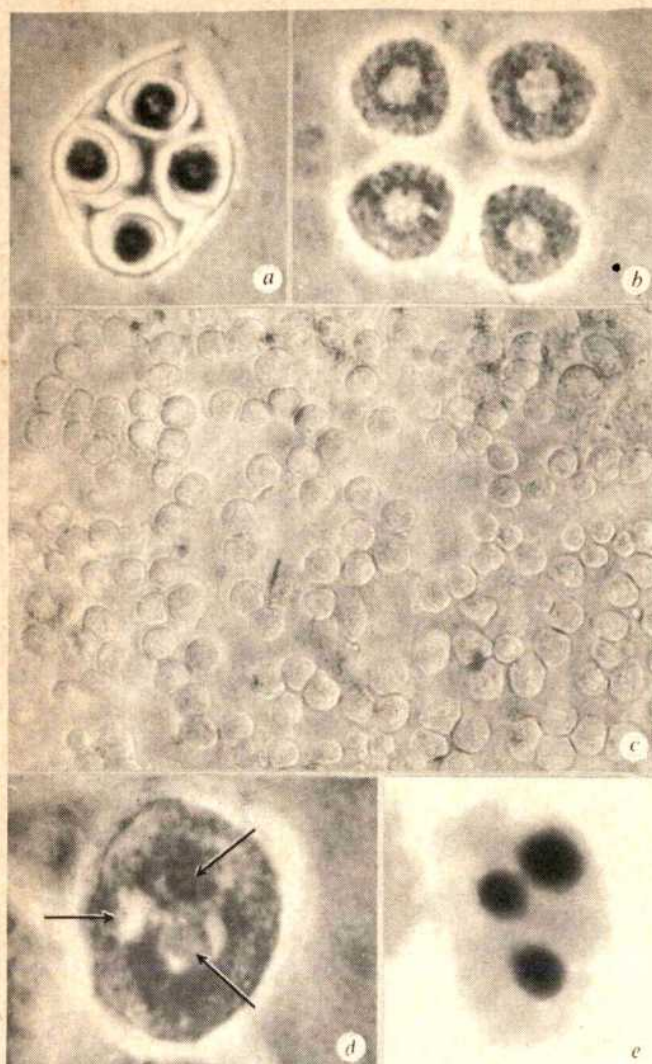


Fig. 1 *a*, Pollen tetrad; observe the massive enveloping wall ($\times 700$). *b*, Group of four protoplasts released from a tetrad; note the dense cytoplasm and large nucleus ($\times 750$). *c*, Pollen protoplasts obtained with cellulase Type II+helicase ($\times 400$). *d*, Protoplast cultured for 5 d showing three nuclei (arrow-marked) without concomitant cell wall formation (phase contrast $\times 1,875$). *e*, A protoplast fixed and stained by carbol-fuchsin method; of the three nuclei one is distinctly larger ($\times 1,875$).

disorganisation and consequent release of protoplasts. The enhanced activity observed with cellulase-helicase mixtures could be due to the complementary and simultaneous action of the enzymes at different sites. That the cell wall composition in the Solanaceae could be species and tissue dependent is further borne out by experiments with somatic cells. Raj and Herr obtained protoplasts from *Lycopersicon*⁴ and *Solanum*⁵ with polygalacturonase, an enzyme that was ineffective in the isolation of protoplasts from *Nicotiana* cells.

The average yield of protoplasts from tobacco tetrads was 35% (ref. 1). In our experiments, the highest percentages obtained were: 29.6 in 1 h, 48.3 in 2 h, 75.4 in 4 h, and 98.4 in 6 h of incubation. The isolated pollen protoplasts were spherical, non-vacuolate and of uniform size, about 10–12 μm in diameter (Fig. 1c). They contained dense cytoplasm and a prominent nucleus (Fig. 1b). Phenomena such as spontaneous aggregation, sub-protoplast formation and budding that are normally associated with somatic protoplasts⁶ were, however, not observed.

The protoplasts were cultured as hanging drops in a modified White's medium. The nucleus in some of the

5 d of incubation, producing three nuclei unaccompanied by cell wall formation (Fig. 1d). One of the nuclei was larger than the other two (Fig. 1e), a condition analogous to the male gametophyte *in vivo* which contains a larger vegetative and two smaller sperm nuclei.

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The Secretion of Migration Inhibitory Factor by Intact Schistosome Egg Granulomas maintained *in vitro*

TUBERCLE formation and delayed type dermal reactivity are the hallmarks of tuberculosis, yet the relationship between the two has only recently begun to be elucidated. Most experts still believe that the tuberculous granuloma is a tissue response to the irritative effect of mycobacterial lipids^{1,2}. While the strength of this concept made it difficult to establish granulomatous inflammation as a host immunologic response^{3,5} Warren *et al.*⁶ showed that the schistosome egg granuloma is a manifestation of delayed hypersensitivity, as demonstrated by anamnestic reactivity, specificity, and transferability with immune lymphoid cells but not with antiserum. It was subsequently correlated with other parameters of the cell-mediated immune reaction, including delayed dermal reaction, lymphocyte transformation and macrophage-migration inhibition⁷. Similar results have been provided for the experimental tuberculous granuloma^{8–13}. Here we report the secretion of a lymphokine by intact granulomas maintained *in vitro*, further confirming the hypersensitivity character of the schistosome egg granuloma.

Intact granulomas were isolated¹⁴ from the livers of Swiss mice (Carworth, CF1 strain) exposed 8 weeks previously to 200 cercariae of the Puerto Rican strain of *S. mansoni*. Granulomas were washed twice with 150 ml of saline and settled in a conical flask. One hundred granulomas were counted into plastic 35 $\times$ 10 mm Petri dishes, No. 3001 (Falcon Plastics, California) and were suspended in 1.9 ml of RPMI-1640 medium (Grand Island Biological Company, NY) supplemented with 10% heat-inactivated normal human plasma, 100 units ml⁻¹ of penicillin, 100 μg ml⁻¹ of streptomycin and 2 mmol ml⁻¹ of glutamine. Soluble egg antigens (SEA) were obtained from homogenised parasite eggs as described earlier¹⁵. The protein content of this preparation was 470 μg ml⁻¹ (ref. 16). For the examination of non-specific reactivity either a mycobacterial culture filtrate (a 10-fold concentrate of *Mycobacterium tuberculosis* strain H₃₇Ra (ref. 17) having a protein content of 5 mg ml⁻¹) or commercial PPD, second strength (Parke-Davis and Co., Detroit, Michigan) was used. Dishes were set up in duplicate or triplicate for each antigen concentration and buffer controls. Supernatants from each concentration of antigen

macrophage migration inhibition using the indirect assay of David¹⁸. Peritoneal exudate cells were obtained from 400 g female Hartley strain guinea pigs after 2 d irritation with Klearol, a light mineral oil. The assay was carried out as described earlier⁷. One-half ml volumes of culture fluids were mixed with the same volume of medium and added to duplicate capillaries in the migration chambers. Preliminary testing of the culture supernatants obtained after the first 24 h of incubation gave erratic and mainly negative results. Results obtained from 48-h supernatants are shown in Fig. 1. Assaying the supernatants has the additional advantage of having minimal residues of human plasma and antigen. Percentage of inhibition was calculated as follows:

$$\% \text{ Inhibition} = \frac{100 - \frac{\text{Average migration of normal cells in supernatants of antigen-stimulated granulomas}}{\text{Average migration of normal cells in supernatants of unstimulated granulomas}} \times 100}{100}$$

Twenty per cent or greater inhibition was considered to be significant.

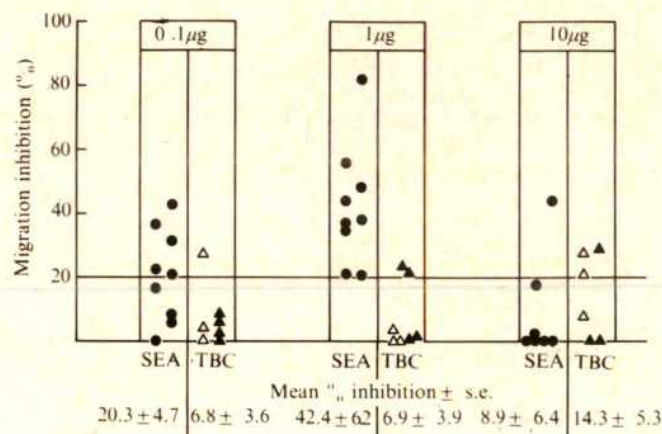


Fig. 1 The inhibition of migration of normal guinea pig peritoneal cells by supernatants from liver granulomas maintained *in vitro*. SEA, Soluble schistosome egg antigens; MCF, mycobacterial culture filtrate; PPD, purified protein derivative.

The isolated granulomas were well circumscribed, compact entities containing one or occasionally more parasite eggs surrounded by fibroblasts, macrophages, occasional epithelioid cells and eosinophils encased in a fibrous matrix. Numerous lymphocytes were visible at the periphery of the lesions, but no plasma cells were seen (Fig. 2). Supernatants obtained from cultures of unstimulated granulomas did not inhibit migration of normal peritoneal cells. SEA up to 40 µg per migration chamber was not inhibitory to the migration of normal peritoneal exudate cells, but both mycobacterial culture filtrates and PPD caused strong (30–50%) inhibition of the migration of cells when added in the concentration of 10 µg per chamber. Thus, the occasional higher inhibitory values of migration seen in PPD or mycobacterial culture filtrate-incubated cultures may be due to the direct inhibitory action of the residual antigens on normal peritoneal exudate cells.

Pooled percentages of migration inhibition showed that incubation of granulomas with 0.1 µg of SEA yielded five of nine supernatants which significantly inhibited the migration of macrophages (mean 20.3 ± 4.7%). Optimal inhibition (nine of nine) was obtained from 1 µg SEA incubated samples (mean 42.4 ± 6.2%) while 10 µg antigen stimulated MIF production in only one of seven samples (mean 8.9 ± 6.4%)

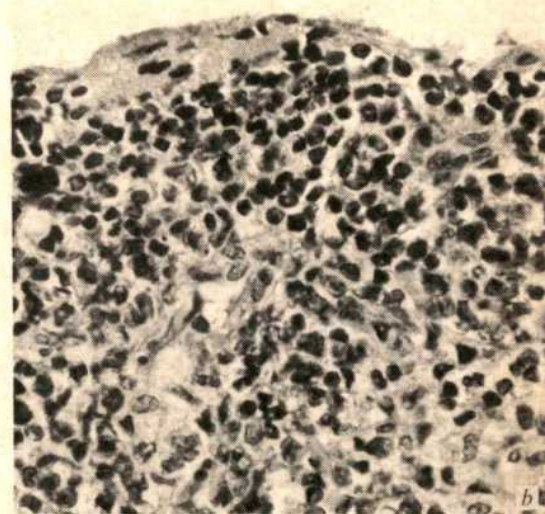
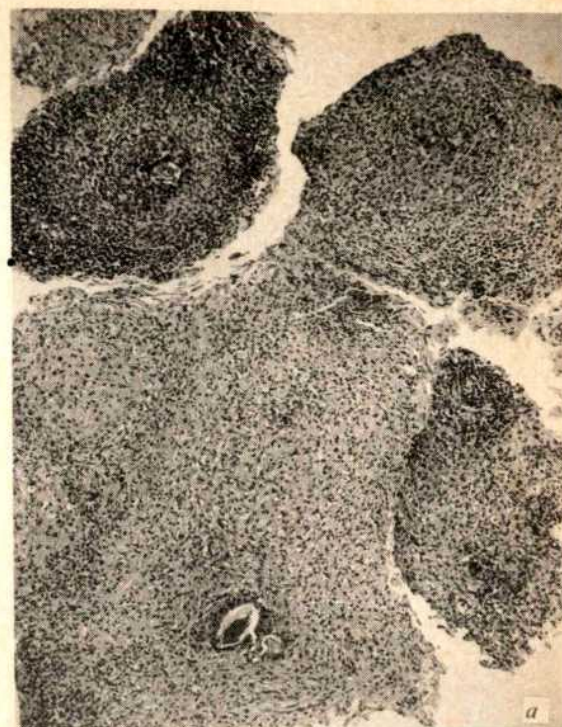


Fig. 2 a, Sections of liver granulomas from mice infected with *Schistosoma mansoni* for 8 weeks. Note schistosome eggs in the centre of several of the lesions. Haematoxylin and eosin × 96. b, High magnification of one of the more highly cellular granulomas, showing predominantly mononuclear cell composition. Haematoxylin and eosin × 384.

Reactions of delayed hypersensitivity are considered to be mediated by a number of soluble substances known as lymphokines^{19,20}. Lymphokines obtained from tissue cultures of antigen-stimulated lymphocytes were shown to elicit inflammatory reactions in normal animals when injected intradermally^{19,21,22}. Recently, extracts of delayed hypersensitivity skin reaction sites were found to possess chemotactic but not MIF activity for macrophages and were shown

animals²³. No information is available, however, on the role of lymphokines in inflammatory reactions such as the granuloma.

The granulomatous inflammation around injected schistosome eggs in the lungs of mice is a delayed hypersensitivity immune response⁶. Also, hypersensitivity-type granulomas have been elicited in mycobacterium²⁴, histoplasma- or schistosome-infected animals¹² following the injection of bentonite particles coated with soluble antigens of these organisms, while bare or heterologously-coated particles evoked small foreign body type granulomas. Using this model it was also shown that infected mice, which otherwise reacted with a foreign body granulomatous inflammation around bare particles, developed florid hypersensitivity type granulomas when systemically challenged with the homologous soluble antigen¹². It was surmised that such a reaction could have been caused by the action of circulating lymphokines liberated by the interaction of antigen and the sensitised system. This was shown recently when a large systemic challenge dose of old tuberculin elicited the appearance of MIF and interferon in the circulation of BCG-infected mice²⁵.

While it has been speculated that mediators such as MIF may be instrumental in the formation of the infectious granuloma^{9,26,27} our results provide the first evidence that the granuloma is an immunologic entity capable of secreting soluble mediators on antigenic stimulation. Preliminary observations using concentrated MIF-rich culture fluids coated onto bentonite particles have revealed that MIF can directly elicit a mononuclear granulomatous response.

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GENERAL

Ignorance about Limitations to Growth

Forrester¹ and Meadows *et al.*² have presented a family of computer models simulating the future behaviour of some world problems which suggest predicaments of mankind caused by compounded growth. Here I report preliminary results from a different pattern of models which imply that more hopeful outcomes are possible. Both models are assailable oversimplifications.

Proposing a different family of models is not intended as a rejection of the predicament position; indeed, for the present purpose of a broad discussions of assumptions, the predicament models would have to be invented if they did not already exist. The vital policy issues of the next few decades require the clearest illumination of alternatives that critical debate can provide, and in this spirit I regret Gabor's view³: "I hope and I believe that these critics will become silent in time for humanity to avoid the danger of perpetual poverty." I also dissent from Gabor's statement that the computer "can stimulate almost every system if we feed the data into it. It is superior to the human mind only in its ability to deal with complexity." The data have to be selected by the use of assumptions, as discussed below.

The Forrester-Meadows models contain five principal variables (population, food, capital, natural resources and pollution), the state of which is taken to represent the physical aspects of life in this world. This is a serious oversimplification, shared by all fruitful models and theories. Relations are set up between these variables, and the models consist of the growth rates, their multiplication and addition to exert effects on chosen points of the network of connections, and delays between original events and their consequences. Altogether, more than fifty items (computer statements) are used in ref. 1, more than 100 in ref. 2. The number of connections chosen in the process of modelling is larger still, and the assignment of quantities to each relation represents further choices. A description indicating why some connections are not made would require accounts of greater length. ("World III", for example, is chosen from over 7¹⁵⁰ networks formally consistent with the set of items in ref. 2.)

A typical example is shown in Fig. 1. Population increases by those born and decreases by those who died. If enough food is available, birth rate increases and death rate decreases. If, under the pressure of population growth, food production lags behind food requirements, the birth rate decreases and the death rate increases. As people once born die after a delay, (life expectancy), adequate food may "drive" the population to numbers prone to starvation ("overshoot" in control engineering terms), high death rate and severe decrease one to two generations later. This "collapse mode" occurs in all but a few highly "planned" sets of conditions (far from "normal" or "free running" or "intuitively corrected" conditions^{1,2}).

Similar "loops" to that of Fig. 1 connect crowding, pollution and the exhaustion of natural resources to "adjust the population to the maximum that food can support". This statement

of the inexhaustible set of the more detailed and technical assumptions in this model family:

(1) "The Malthusian thesis: . . . population is regulated to the food supply" (ref. 1, p. 27) and "the apparent goal of the world system is to produce more people with more (food, material goods, clean air and water) for each person" (ref. 2, p. 86).

(2) No regulatory mechanisms anticipate the Malthusian disaster—hence the predicaments.

Analogous assumptions are made about mounting world use of materials, pollution and crowding to the point of distress. Because both world history, demographic science, economics and the emerging concern for pollution and crowding are rich in varieties of theories, observations, conclusions and opinions, authorities can be found to support almost any assumption.

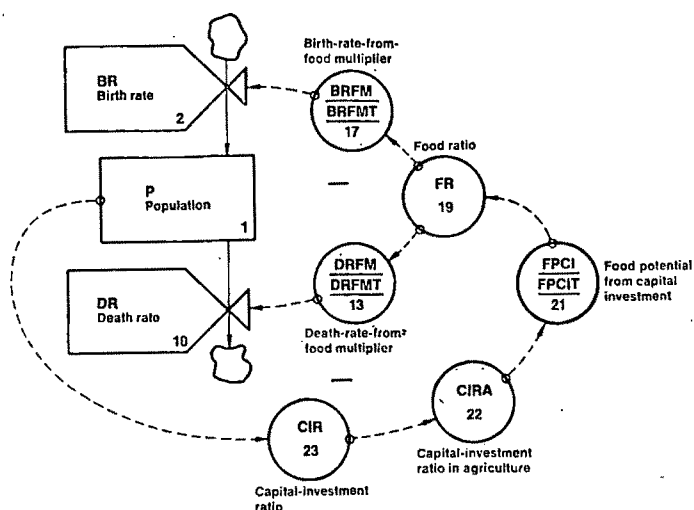


Fig. 1 Negative feedback in population control—after Forrester¹. Malthusian control: "negative loops that adjust population to the maximum that food can support".

No claims were made that refs 1 and 2 forecast world behaviour, or that they have been adequately refined. Yet disturbing implications are drawn from the model behaviour, and offered as cause for world, and decision makers', concerns and future actions.

In addition to the school of neo-Malthusians among demographers prepared to theorise on mechanisms of, and future trends in, population (seemingly a minority of all demographers), there exists another school which emphasises "demographic regulation" and "demographic transition". For the work described here, my chief source has been Bogue⁴; unless a specific reference is given all demographic information has been taken from his work. Errors of selection and interpretation are, of course, my responsibility.

The notion of demographic regulation implies that, in the past (and therefore possibly or probably in the future), adaptation has produced (and, it is hoped, will again produce) conditions of population stability in which a large part (sometimes almost all) of mankind was free from hunger without reacting with rapid population growth. Again, as in the Malthusian thesis, examples abound without being conclusive. (Samoa, the experience of many but not all developed countries to the 30's of this century, etc.) They are reinforced by partial evidence (or conjectures) arising from very early human pre-history, and much evidence from the animal world⁵. Demographic transition implies that such decreases in death rate as are almost world wide are followed, within one to three generations, by corresponding declines in birth rates, bringing population growth back to "manageable" levels.

doubling times of seventy to several hundreds of years. This set of theories has as many critics as the neo-Malthusian theories, and I use it as an undefended assumption. Clearly this pair of notions implies the exact opposite of assumptions 1 and 2 above.

Analogous assumptions are made about natural resources use and pollution: that, early enough, learning of recycling and substitution will forestall disaster in the natural resource sector, and that similar learning rates will rescue us from choking in pollution (pollution is also almost discounted in ref. 2).

Again, I do not defend these assumptions. I merely point out that some of today's key natural resources were not used 100 yr ago, and that many key resources of 100 yr ago have lost this status, such as charcoal, wood as fuel or ship-building material, and horses for transport in developed countries. Such substitution is likely to continue.

The most frightening dangers from pollution arise from uncertainty, as in the DDT chain of effects. With less than 1 part in 1,000 of past production of this pesticide yet active in the biosphere, many sudden bio-ecological disasters have occurred¹⁸. But I refuse to attempt a model of sheer uncertainty for policy guidance.

A further assumption is that of saturation of demand for any specific good per person, accompanied by gradual increase in productivity in developing conditions. This is consistent with refs 7 and 8 and much else since Engel's law of a 100 yr ago. It implies that, at some stage of development, labour is displaced to more and more "advanced" sectors of an economy, according to its taste for each tradeoff, progressively remote from primary needs. This is not unlike references^{1,2} to "global equilibrium", though built into the model at the beginning.

Finally, I assume that the use of this model will be for decision makers concerned to investigate if, from any given starting position (whether now or later) there is at least one feasible path to avoid any condition they define as "disaster". If a broad enough range of feasible paths exists (I believe that, as yet, this seems to be the case) much latitude for choice (in local jurisdictions) still exists, and can be optimised locally. Where possible, I prefer simple local models for ready aggregation to those requiring central decisions.

Having chosen a different school of demography as a source for key assumptions, as I turn to data I face the question how, in this age of science, such diversity of theories can co-exist. Data outside the developed countries before the Second World War are uncertain, and even fairly short term projections were wrong for England and Wales⁹. Population estimates for AD 2000 made in the 1920s have been overtaken and increased to around three to four times the original. Particularly for the large population masses of India and China, the cautions of refs 9 and 10 apply in full, and the comments in ref. 11 are surely optimistic.

Thus demographers have reserved the use of their most refined methods for comparisons between different countries at the same time or over the very short period (1950–1970) for which consistent data can be claimed^{4,5,8,12–14}. Transition models have emerged from some of these studies, but⁴ until the 1980 group of census data is available, no empirical resolution of the transition issue is possible. Even more, firm assignment of causes to population growth patterns seems entirely speculative. I discuss the uses made of these imperfect data on the basis of Fig. 2.

In Fig. 2a, approximate plots are shown for the vital statistics (crude birth and death rates) of France, Japan and Taiwan—the last two with speculative estimates from 1970 to about 2050. Both the fall of death rates (by now essentially world wide) and of birth rates (where it has occurred—and that, compared to biological capacity, has been argued to be almost global) have been more rapid the more recent the observation. Yet this speed-up is more conspicuous for death rates as well as

Malthusian mechanisms at work in the underdeveloped world, though very fast growth is occurring at present.

Birth and death rates in Europe at the time of Rome were each about 42 per 1,000. For stable populations, a lower death rate could lead to much higher growth rates than seem to have occurred before "transitions" (doubling times over 1,000 yr) except for short periods, locally. Higher birth rates were inconsistent with data but also biologically improbable because of the short fertility span of women. Lower birth rates would have led either to rapid extinction or, if reversed by corresponding increases in average food supplies or health, to a regain of the earlier values. Thus the "Malthusian trap" seems to have been homeostatic, except for fluctuations due to plague and drought.

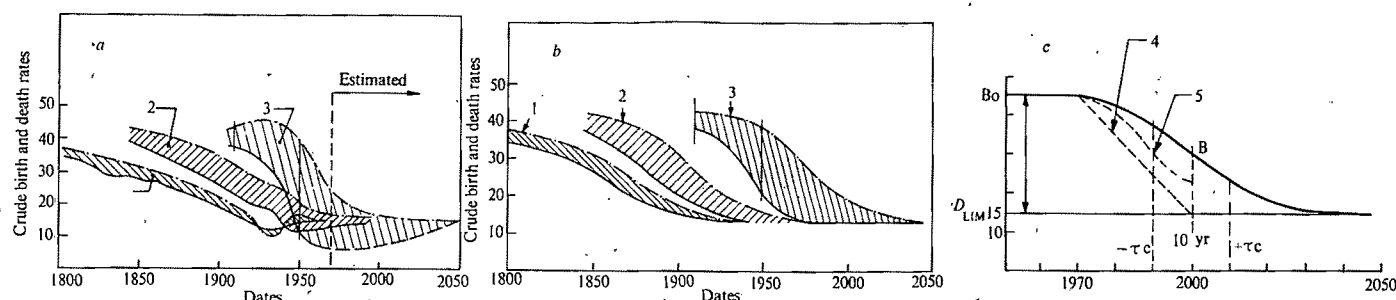


Fig. 2 History of population growth rates in transition: from data to model. —, Deaths; — · —, births; 1, France; 2, Japan; 3, Taiwan. *a*, Data on growth rates (shaded areas) from France to Taiwan; *b*, Fermi function for *a*; *c*, Fermi function and its parameters for growth rate and constant death rate. 4, Bogue's projection 1970–2000; 5, UN projection 1970–2000; B, sample birth rate model.

In Fig. 2*b* I show how each of these patterns of vital statistics has been idealised for computation. In spite of the higher rates of change of the crude vital rates, the birth rate fall seems increasingly delayed, from 20 yr average in France, to 35 yr in Japan, to 50 yr in Taiwan. This is chiefly an artefact of selection of the three "prototypes": the inclusion of the European average¹⁴ would have shown 60 to 70 yr, but its overlap with Japan would have obscured the figure. The principal simplification is the omission of the "undershoot" of death rates. The raw data for Taiwan, for example, have death rates of about 6 to 7 per 1,000 since 1963. For a stable population, this requires a life expectancy of 150 yr. For modelling, this transition phenomenon was incorporated in the difference between rates. This implies that the modelled death rates are close to "intrinsic" death rates, but that growth rates are kept "crude". The modelled "birth" rates have no close demographic equivalent.

Each of the curves in Fig. 2*b* is of the form

$$\begin{aligned} \text{CBR}_\tau &= (B_0 - 15) (1 - 1/2 \exp [(\tau - \tau_0)/\tau_c]) \\ &\quad \text{for } \tau \leq \tau_0 \\ \text{CBR}_\tau &= (B_0 - 15) (1/2 \exp [-(\tau - \tau_0)/\tau_c]) \\ &\quad \text{for } \tau \geq \tau_0 \end{aligned} \quad (1)$$

where B_0 is the initial birth rate, τ_0 the date of the inflection, τ_c the time constant.

This is similar in values to the more familiar "logistic" curve, but simpler to compute, and easy to adapt if the particular situation appears to require an unsymmetrical decay, by adding one more to the three parameters required. I show the final model simplification in Fig. 2*c* where the death rate has been eliminated. Fig. 2*c* is a direct model of the population growth rate, and its relation to the empirical vital rates is obscured—yet not to the extent of the uncertainty of predicting growth rates into the next century. The assumed constant death rate of 15 would require a world life expectancy of 67 yr over the forecast period. The likely rate of change in life expectancy (80 yr seems optimistic) does not affect my

conclusions. The model is less optimistic than either ref. 4 or the UN 1968 "medium" forecast.

The food model has been based on similar mathematical transition curves as Fig. 2*c* and equation (1), but starting at a low initial asymptote and reaching an upper limit, specified near the best fed European dietary levels in grain equivalent calories; this is almost twice the present world average. For the present, distribution questions within each modelled area are neglected. Increase in food per capita is assumed to arise mainly from intensified agriculture, but in China and India some increase in arable land has been assumed.

I am now in a position to discuss briefly the computer runs partly shown in Fig. 3*a–f*. I assume that if trade becomes more significant (the reverse seems true at present), it will be to the

general benefit if it persists. The pattern of change in population growth was assumed to follow equation (1) with $\tau_c = 10$ yr. This assumes a "transition" to proceed from 90% ($B_0 - 15$) to 10% ($B_0 - 15$) in some 3 generations, between the Japanese and the estimated Taiwan prototypes. The inflection point was estimated crudely from such data as could be gleaned^{4,15} on vital rates for the past 10 to 20 yr¹⁵. Food increases were then adjusted to two constraints: that their slope should match, in per capita terms, the slopes in ref. 11 (p. 4), and that τ_c for food increase should be 15 yr (slower than population change transition) if a feasible fit could be found by simulating changes in τ_0 . This did not prove workable in the case of India, but the demonstrated success of the "green revolution" in terms of yield per acre seemed to justify a use of $\tau_c = 10$ yr for that subcontinent.

Both in terms of future growth prospects and food limitations, India–South Asia is the world's most worrisome area. The first food "peak" is the result of modelling the "green revolution", but not its labour disposal problems. I believe that the amount shown is feasible, but that it would not be chosen. Unemployment or distribution problems are signalled by this feature in the model.

The intent of these very simple models is neither to forecast, even implicitly, the levels reached in either population or food, or to forecast "normatively", to set a target and then to deduce what is needed to achieve it. The question here is much more restricted: given assumptions about population, is it necessary to assume agricultural expansion rates and levels, as well as learning rates that are clearly unachievable? If, on the contrary, such improvements have been obtained in the past, then it is assumed feasible to do so again elsewhere. The pattern of population growth may be capable of greater control than here assumed—then greater latitude exists to deal with food more deliberately and with lower stress on world ecology. My pattern of simulation is only concerned with disclosing "feasible regions" (see refs 6 and 19).

In refs 1 and 2, natural resources played key roles. I assumed above that for gross effects, perceiving and learning early could help us avoid disaster from these major variables. In

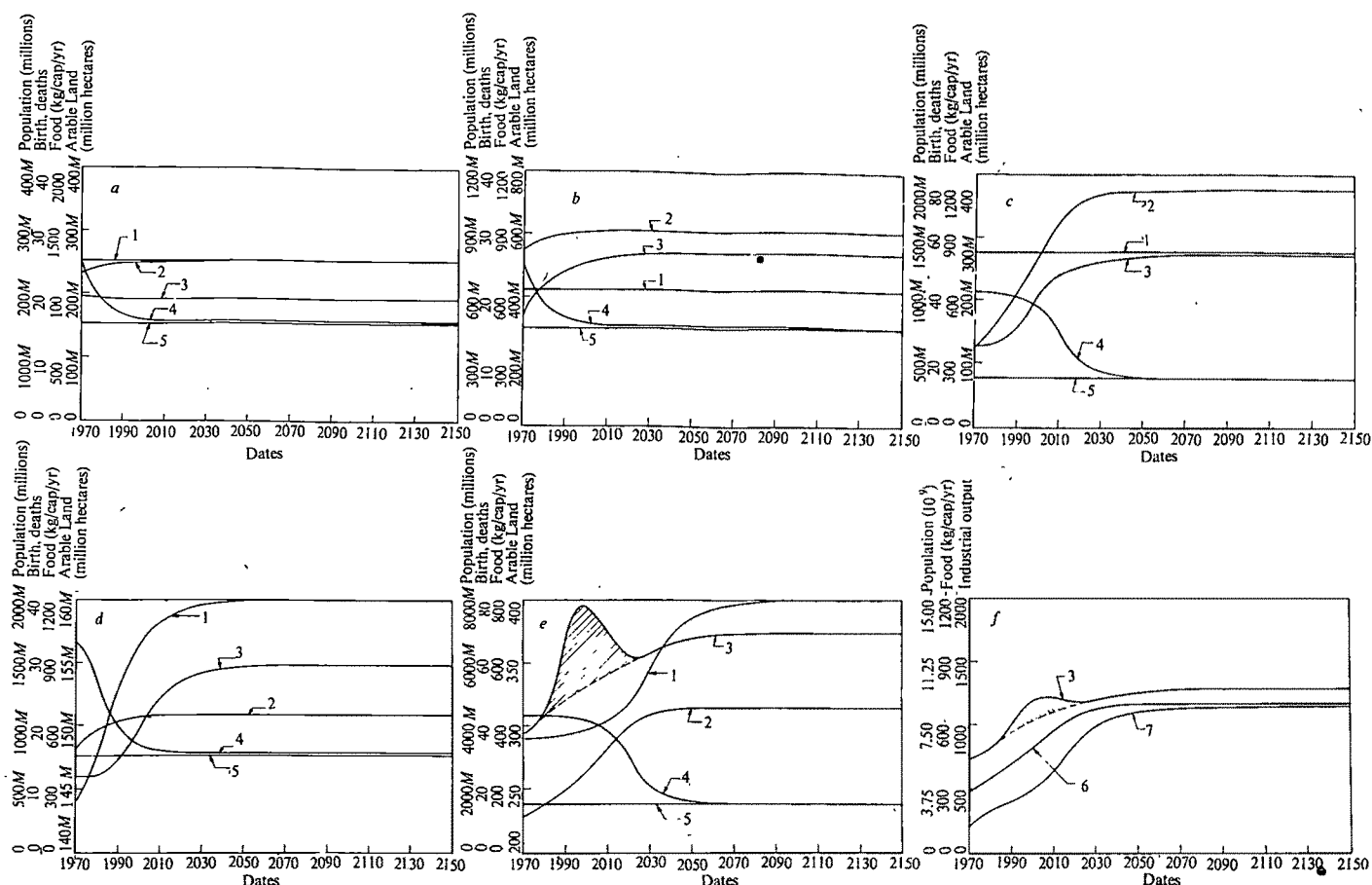


Fig. 3 Feasible food supplies, for modelled populations, in five regions. *a*, North America; *b*, "extended" Europe (including USSR, Japan, Australia and so on); *c*, South America and Africa; *d*, "extended" China (including UN "East Asia"); *e*, "extended" India (including UN "South Asia") and shaded "spurious" area; *f*, summation of *a* to *e* with shaded "spurious" area. This simple addition neglects international trade, at the moment negligible between these groups (except perhaps Europe, the United States and so on, and South America and the developed countries) compared with the uncertainty of data and even more of projections. 1, Arable land (10^6 hectares); 2, population (10^6); 3, food per capita (kg/yr grain equivalent); 4, modelled birth rate per thousand; 5, intrinsic modelled death rate per thousand; 6, population (10^6); 7, industrial output per capita (nominal scaling, \$/yr).

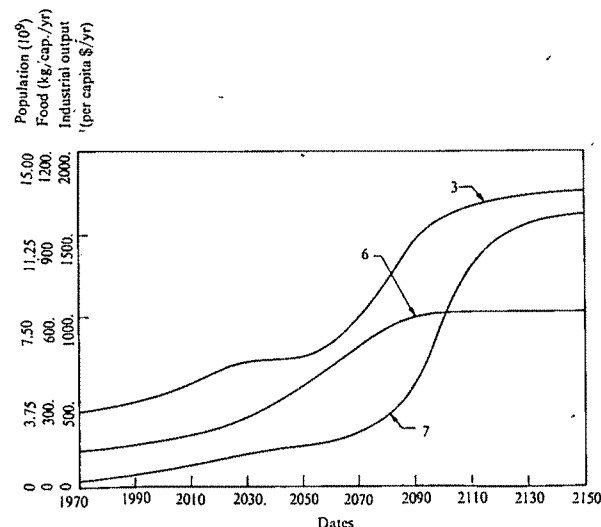
making this assumption, I do not have to presume an exponential or even faster growth of knowledge: for many of these issues, knowledge exists, and as only finite increments of population need be served, the needed increment in knowledge is modest. Its expense may, in fact, lower the future demand in the third world for particular goods now thought desirable in developed countries. Again quite crudely, and assuming multiplier functions opposite in sign to equation (1) for learning but like equation (1) for saturating demand for natural resource intensive industry^{7,8}, I have run the model for each sub-continent and found the increases in "demand" to be "staggered" over several decades (summarised in Fig. 3f). On a similar basis, I have made parameter and policy changes in the model of ref. 2 and have obtained stable and feasible (though different) values (Fig. 4).

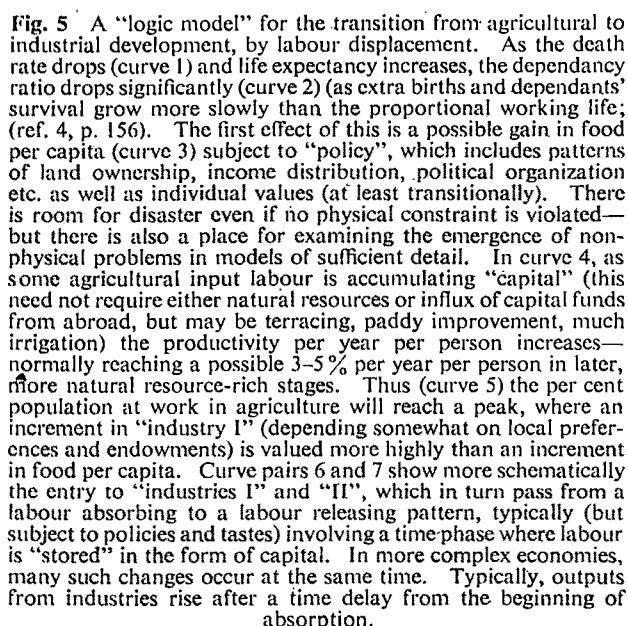
Again, no forecasts are implied, but the question is posed: is it inconceivable for us to learn in time? The answer, that it is conceivable, means that more detailed investigations including local preferences and policy choices have a feasible possibility region to explore in medium range studies. These may be urgent: as each decade passes, the progress of events modifies what remains feasible. The principal question is: How may the most rapid solutions be found?

One of the less obvious results of the decrease in death rate (Fig. 2) and its discussion is the disproportionate increase in the average working life span. With life expectancy of 40 yr the working life is 25 yr; but a 24 yr life expectation corresponds to a working life of only 9 yr. Thus in recent years, the pos-

become an increasing problem. The number of people is a conservative measure. Thus they provide a better measure of events than money in early stages of development, where exchange has not reached major population groups, or in comparisons across great differences of development¹⁶.

The extensions proposed to the sub-models presently





Implications of anticipated extensions based on prior work are: (a) As dependency ratios drop, food output per person can increase (as it appears to have done in the past 5 to 15 yr). Further increases can readily come from accumulation of

I thank Mr R. Ritchie for discussions, Mr G. Berry for computational assistance, Professor D. L. Meadows for details of one of his models, the referees for suggestions, and the Waterloo Faculty Research Fund for financial support.

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Nobel Prizes for Oxford Authors

Oxford University Press warmly congratulate Nikolas Tinbergen and Karl von Frisch on being jointly awarded, with Konrad Lorenz, the 1973 Nobel Prize for Medicine. In their work – Professor Tinbergen's on birds, and Professor von Frisch's on bees – they had, said the citation, revitalized the study of animal behaviour.

The books by Professor Tinbergen in Oxford's list are *The Study of Instinct* (£2.75), 'indispensable to all serious students of animal behaviour', according to *Nature*; *Tracks*, illustrated by E. A. R. Ennion (£2); and *Signals for Survival* (£2). The last-named, written jointly with Hugh Falkus and with illustrations by E. A. R. Ennion, describes the sign-language of the Lesser Blackbacked Gull.

In *The Dance Language and Orientation of Bees* (£6.50), Karl von Frisch describes the fascinating discoveries made during fifty years of study. 'The book is an object lesson in patient and skilful observation coupled to ingenious experimental technique.' – *The Entomologist's Record*. It is published by Oxford for Harvard University Press.

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BOOK REVIEWS

Science and Capitalism

Autocritique de la Science. Edited by Alain Jaubert and Jean-Marc Levy-Leblond. (Collection Science Ouverte.) Pp. 383. (Editions du Seuil: Paris, 1973.) n.p.

It is no longer particularly original or bold to cry out against science and its misapplications. This collection of characteristic texts, mostly of French origin but many translated from English and several from Italian, is significant mainly because it attempts a comprehensive attack from the standpoint of revolutionary socialism. The material is drawn from articles, speeches and pamphlets written by scientists for other scientists on topics ranging from military research to the underemployment of women. With styles ranging from the purest Cartesian analysis to a call for strike action against the *patron* of a *labo*, it is difficult to achieve a unified approach, but the editors have chosen shrewdly and have set each piece in context with a brief introduction. The book can, therefore, be read not only for the individual texts but as a reasonably well balanced exposition of the point of view of a small but not insignificant fraction of the scientific community in France and many other Western nations.

The ideological framework is explicitly Marxist. But there is little evidence of a deep and thoroughgoing analysis of the role of science in contemporary society. An attempt to revise the theory of surplus value to cover scientific work runs away into the sands, and Roqueplo's incisive "eight theses" succeed admirably in not distinguishing between capitalist and socialist science. For most of these authors (including the editors) it seems that a primitive conception of the class struggle and a gut reaction in favour of the correct side in various wars (especially Vietnam) are sufficient ideological justification for political comment and action.

This simplification of the historical and sociological background is a grave defect in the discussion of the militarisation of research. It is easy to renounce financial support from defence organisations and to denounce academic scientists who put themselves at the service of the soldiers in a manifestly unjust war. But the roots of gangsterism, tribalism, patriotism, and nationalism are not nourished exclusively by capitalism: and a brief reference to "state capitalism" does not deal adequately with science in the Soviet Union, for example, which is equally regimented

Other noxious applications of science and technology are also interpreted as obvious consequences of the devotion of the capitalist ruling class to the maintenance of their power and profits. But several forceful theoretical papers at the beginning of the book make much of the practical incompetence of technocracy and of scientism. In their political and economic analysis the authors attribute too many of our present follies to clever conspiracies by the power élite, and do not allow sufficiently for the misplaced but universal popular belief that social problems can be solved by specialist skills and technical expertise. This applies particularly to the state of science in the Third World, where much more positive thinking is needed about how to bring genuine scientific benefits to the people. Bad education in and about science can certainly be blamed, but cannot itself be entirely explained away as a reflection of class domination.

Coming nearer home, the discussion of the actual position of the scientific worker is much more realistic. Whether or not this exemplifies the Marxian prediction of the general proletarianisation of the professional classes ("lackeys of the bourgeoisie"?), the increasing exploitation and repression of the individual scientist in the era of bureaucratic big science is a very significant phenomenon, whose psychological and political consequences are vividly depicted in these pages. Some of the current problems emphasised here, such as the gross abuse of power by research bosses, are exacerbated in France by the peculiar organisational structure of universities and scientific institutes, but we must not be complacent about such serious issues as graduate unemployment, the equivocal position of graduate students, uncertainty of tenure amongst research workers, the subordination of skilled technicians, etc. Here again, the plea for solidarity in the face of the class enemy does not resolve all questions. The relationships between an élite of *mandarins* and the body of younger *scientifiques* from whom they have been selected by harsh competition are not exactly equivalent to those between capitalist and worker, and belong more to anthropology than to political economy.

Perhaps I have said enough to show that "self-criticism" of science is an essential activity, by which many matters of the most serious concern can be brought to light. But to point a finger of bitter censure at a scandal, a crime, or an injustice, is only the first step. An

as well as of science—demands an eye for relevant evidence, an open mind towards many theoretical possibilities, and perhaps a little more of the intellectual modesty and scepticism that scientists are themselves supposed to acquire through practising their profession.

JOHN ZIMAN

Irradiating Bone

The Effects of Irradiation on the Skeleton. By Janet M. Vaughan. Pp. xvi+297. (Clarendon: Oxford; Oxford University: London, March 1973.) £7.75.

THERE is now a large body of information on the important and, at times, emotive subject of the effects of irradiation on bone. This has appeared for the most part in the regular journals but considerable numbers of researches have been published in books reporting the proceedings of specialist conferences. In her book, Dame Janet Vaughan, herself a researcher of great distinction in this field, has brought together these scattered and largely uncoordinated researches into a well informed and balanced synthesis. The book is written from the biologist's viewpoint but has the merit that the biological findings and the physical properties of radiation are related in an unusually perceptive way. The result makes rewarding reading for those in both the biological and physical sciences.

At the beginning of the book the nature of radiobiological action and the characteristics of ionising radiations are dealt with briefly, with consideration of the structure and physiology of the skeleton that are relevant to the irradiation of bone. There follow two chapters discussing in detail the tissues of bone that are at risk, the types of radiation induced cancer that can arise, and the sites of the tissues of tumour origin. A chapter is devoted to the effects of external irradiation, analysing the evidence, for example, of leukaemia induction in human populations, and the problems of internal irradiation are then considered generally in chapter 6.

A most important part of the book deals individually, in separate chapters, with the well known bone-seeking radionuclides: radium, with the dramatic series of radium poisoning cases that occurred mainly in the earlier decades of this century; the strontium isotopes; the isotopes of plutonium, americium and thorium that are deposited on bone surfaces; lastly radiophosphorus and other less known and less used radionuclides. One of the most useful

of some 700 papers, quoted with full titles, together with the page numbers in the text to which they refer. This is far more useful to a reader than an author index.

The book is written with great lucidity and is well produced with only very few and very minor misprints apparent. The synthesis achieved in this book will be a most valuable asset to those actively working on bone, but it should have a wider appeal in other fields, for example in nuclear medicine, radiotherapy, cancer research and radiation protection. This work will remain an authoritative and enlightening guide to the long term researches that are going on in many laboratories on the effects of skeletal irradiation.

F. W. SPIERS

Animal Sociology

Organisation in Animal Communities: Experimental and Naturalistic Studies of the Social Behaviour of Animals. By Hilary O. Box. Pp. 251. (Butterworth: London, March 1973.) £5 cloth; £2.50 paper.

THIS book, which grew out of a course of lectures given to psychology students at the University of Reading, touches upon a wide range of behavioural phenomena which can loosely be described as social in the sense that in some way they concern interactions between animals. There are descriptions of the social life of many animals and the book is a quite useful, although cursory, account of some of the work which has been done on social behaviour. "Social" is taken very broadly, and mimicry and parasitism are among the subjects undertaken. In addition there are sections on the influence of early experience, particularly deprivation of various sorts, on subsequent social responses, a chapter on communication and a brief survey of the social behaviour of some domesticated animals. The effects of overcrowding and the role of behaviour in the determination of animal numbers are also discussed.

Detailed and comprehensive coverage of all these topics is clearly impossible in only 251 pages, but even with this space limitation, one would have thought that there should have been room to discuss certain important questions which are in fact omitted or not faced squarely. For example, it is surprising that in a chapter which compares insect and human societies, there should be no mention of the fact that the apparent "altruism" shown by many of the social insects is probably related to the uniquely close genetic relationship between individuals in a colony¹. To say that "We now accept that social

petition and mutual aid" (page 6) without discussing such variables as the degree of genetic relationship within a social group simply sidesteps important questions of how natural selection works.

In short, this book has been written by a psychologist, and it shows.

MARIAN DAWKINS

¹ Hamilton, W. D., *Am. Nat.*, 97, 354 (1963).

Limited Omnivorousness

Seed to Civilization: The Story of Man's Food. (A Series of Books in Biology.) By C. B. Heiser jun. Pp. xii+243. (W. H. Freeman: San Francisco and Reading, July 1973.) £3.60 cloth; £1.50 paper.

MAN can appropriately be described as omnivorous. Nevertheless, like other animals, his selection of food is influenced by the complex web of compulsions by which his behaviour is moulded. That is to say, he is subject to the natural history of the species. This is as true today as it ever was. As Professor Heiser points out at the beginning of his book, there is no reason to assume that we are any more intelligent now than were the people who invented agriculture ten thousand years ago. It is, therefore, not surprising that even after having described, for the benefit of the general reader for whom this popular exposition is intended, a varied selection of fact and opinion he reaches the conclusion that "the explanations of why and how man 'invented' agriculture . . . are far from certain".

The valuable substance of the book is contained in the chapters in which the origin as human food of the species of animals and plants selected for domestication is described. There is an interesting narrative of what is known of the dog's becoming in 8400 BC man's dumb friend, with a charming illustration of a clay figure from Mexico of a dog specially fattened on maize for the table. The history of the sheep as mutton goes back eleven millenia and the goat about as far. Cattle came later although aurochs, it seems, were worshipped for a long time before they were eaten. The stories of the more exotic animals, the turkey and the Muscovy duck from the Americas, the guinea pig, and the llama from Peru, are narrated as well. It is not surprising that Heiser, a botanist, devotes forty-eight pages to an excellent chapter about grasses, ranging from wheat to bamboo. This chapter, like the rest of the book, is well illustrated with drawings and photographs from many parts of the world and many periods of history. Other chapters deal with legumes, roots,

the Cruciferae, comprising a dozen forms from cabbages to rutabaga, with gourds, nuts, coffee and pepper.

All this is informative, interesting, wide-ranging and well suited for the students of general biology, economic botany, anthropology and home economics at whom, according to the publishers, the book is aimed. A three-page chapter about nutrition is less satisfactory and seems a whit perfunctory. That the only table in it should be of the amino acid contents of various proteins owes more to today's fashion than to the major priorities of physiological need. But it is in his last chapter that we leave behind such delights as the account of the breadfruit, *Artocarpus altilis*, and the troubles that Captain Bligh encountered in transporting 1,000 young breadfruit trees from Tahiti to the West Indies (he succeeded in the end). Instead, there come the all-too-familiar ill-thought-out adumbrations about the population explosion and the "corrupt, inefficient and unstable governments" from which hungry nations suffer. There are quotations from strings of those pessimistic books, mostly written by chemists and biologists, about what "government" should do to succour developing nations. Not everyone agreed with all the rude things that Professor Wilfred Beckerman had to say about the blunders of chemists and biologists when they ignore the existence of political economy as a well established discipline in its own right; but enough of them were sufficiently incontrovertible, one would have thought, to discourage otherwise well-judging authors like Professor Heiser from allowing their feelings to draw them away from the topics upon which they are worth reading to the ritual obeisance to the starving millions.

MAGNUS PYKE

Development

Developmental Biology: Its Cellular and Molecular Foundations. By Maurice Sussman. (Foundation of Modern Biology Series.) Pp. xvi+297. (Prentice-Hall: Englewood Cliffs, NJ, and Hemel Hempstead, March 1973.) £3.50 paper.

DR SUSSMAN's book is written in an engaging and buttonholing style that has the vigour (and the jokes) that will be familiar to those who have heard him lecture. This inimitable style is admirably suited to his purpose which is to demonstrate "the extraordinary power of science as a method of asking questions properly and answering them with rigour." Much of the book is written in the Socratic tradition as interpreted by modern molecular biologists and provides an excellent and compelling intro-

the fundamental aspects of developmental biology. There is a danger, of course, that the beginning student (who is admirably catered for with two introductory review chapters) may not realise that what is being presented is a particular point of view. The preface makes this quite clear but I would have liked to see, perhaps in the bibliography which is given at the end of each chapter, some reference to opposing viewpoints to counter the somewhat dogmatic tone of parts of the text. I doubt, for example, if all would agree that "the only reasonable interpretation" of Dr Mintz's experiments on allphenic mice is the one that she has suggested; and the treatment of morphogenetic fields is curiously old fashioned. These are, however, minor criticisms of a book which can be recommended to both undergraduate and postgraduate students and which will be invaluable as a source-book of provocative and pungent statements for those who organise seminars and set examination papers.

J. M. ASHWORTH

Bird Biology

Avian Biology. Edited by Donald S. Farner and James R. King. Taxonomic Editor: Kenneth C. Parkes. Vol. 2. Pp. xxiii+612. (Academic: New York and London, December 1972.) \$32.

SOME ten years ago, A. J. Marshall edited two volumes on the biology and physiology of birds. This volume is the second in a series of three which provide an updated and much needed replacement for Marshall's work. There are new editors, almost all new authors, a different organisation, and more complete coverage.

The volume at hand (volume 2) has three chapters dealing with feathers; the remaining six deal with specific physiological systems such as respiration and circulation. This selection can best be evaluated in the context of the complete series. Volume 1 (already published) has four chapters of more or less classical ornithology and seven oriented towards ecology. Volume 3 (to be published) will deal with reproduction and endocrine systems (four chapters), and with senses and behaviour (another four chapters).

Does this cover the area of avian biology? One could instead ask, what are the most characteristic aspects of bird biology? It seems that these are (1) birds are warm blooded and have feathers, (2) they fly and migrate over long distances, and (3) they have a characteristic mode of reproduction. Some of these subjects are well covered; feathers have three chapters of volume 2, and reproduction will come in volume 3. But there are no individual

or on thermoregulation. I find a lack of balance here, for endocrinology will have three chapters, and substantial sections on endocrinological control will appear in two more.

Volume 2 contains nine chapters which, as can be expected, are of uneven quality. Most presentations are good and a few are outstanding. Some could be criticised. Chapter 2, ("Patterns of Molting") is from the beginning steeped in terminology which is poorly or not at all defined, and is difficult to follow for a non-specialist. Chapter 7 ("Nutrition") is, as the author states, restricted mainly to the domestic chicken. True enough, most nutritional studies on birds are on chickens, but nevertheless I see no need for the extensive discussions of animal husbandry and the many tables on the nutritional value of commercial feed ingredients. A stronger editorial hand would have been helpful for this chapter, and for the following one ("Intermediary Metabolism"), which seems to be well organised and contains much information but suffers from lack of perspective. With these items to criticise, we are left with a volume that contains mostly good and excellent papers.

There are separate indices for author names, for bird names and for subjects. The publisher deserves praise for making these very helpful tools available to the worker who uses the volumes for constant reference.

KNUT SCHMIDT-NIELSEN

Elementary Particles

Particle Physics: An Introduction. By M. Leon. Pp. xii+268. (Academic: New York and London, March 1973.) \$14.50.

PARTICLE physics is a very difficult subject to teach at introductory level. It has a vast glossary of jargon and there is a large set of intriguing and profound data. But the theoretical framework, which will one day unify the subject, is still lying about as a kit of parts. The kit may be almost complete, but no one has been able to put it together.

This book treats the main theoretical components in an admirably concise way. There are reasonably thorough treatments of scattering theory and quantum-field theory, with brief discussions of quantum electrodynamics, hadron dynamics and weak interactions. Particle properties are presented, with emphasis on symmetries, including SU(3). Such recent developments as dual models, or unified weak and electromagnetic theories, are quite rightly omitted.

Although the preface claims that this text is useful for "seniors and graduate students", the material is too advanced

probably inevitable in a book which covers so much of the theoretical kit. A sensible starting point for undergraduates is the much more experimental book of I. S. Hughes (Penguin library of physical sciences). For first-year postgraduates, however, this book promises to be extremely useful.

DAVID J. MILLER

Neonatal Anatomy

Functional Anatomy of the Newborn. By Edmund S. Crelin. Pp. xii+87. (Yale University: New Haven and London, February 1973.) £3.50 cloth; £1.75 paper.

THIS somewhat dry and colourless book is an attempt by an anatomist to provide "a concise guide to be used by all personnel involved in one form or another with the newborn infant, including students". The author is a consultant to the Newborn Special Care Unit at Yale and assists in the evaluation of newborn infants with birth defects.

This book has a mere seventy-one pages of text and only three illustrations. These are line drawings by the author, one illustrating all the ossified parts of the skeleton in the full term newborn infant, the second a sort of see-through, half frontal, topographic anatomy of the full-term newborn infant, and the third a mid-sagittal section.

There is no subdivision into chapters or sections, but sequential descriptions of various tissues or organs. The order is based on that of the larger atlas produced by the author a few years ago.

There are some potentially useful statistics in the text, but it is difficult to see of what practical value much of the information can be to the practising paediatrician, pathologist or obstetrician. Thus, the opening section on body weight, size and proportions states that "the average full-term infant (8½ months) weighs about 3,300 gm (7 lb) and the average crown-heel length is about 50 cm (20 inches)", whereas "a premature newborn infant (7 months) weighing only 1,200 gm (3 lb) would have a crown-heel length of about 38 cm (16 inches)". No information is given for any other gestational age. How much more useful would have been a table or graph showing the increase in weight and length with gestation.

Throughout the book there is very little reference to the functional anatomy at various stages of gestation.

Occasional sections do have a few useful details, with some of the implied clinical applications. Thus the development of the lung and its structure is done in some detail and includes comment on surfactant; and the cardio-

detail. In contrast the epidermal ridge pattern of the fingers and palms is dismissed in a single comment that they are unique to the individual, and the section on the brain has practically no comment on its changes during foetal development.

This book is difficult to read as a continuous text, and as a source of reference I think people will prefer the more comprehensive neonatal clinical texts available on various systems.

VICTOR DUBOWITZ

Nutritional Technology

Introduction to Food Science and Technology. By George F. Stewart and Maynard A. Amerine. Pp. xiii+294. (Academic: New York and London, January 1973.) \$12.50.

Food science differs from other sciences in drawing on a wider range of disciplines for its techniques; the authors have done well to cover most of them in less than 300 pages. Each chapter is a wide ranging survey of a subject starting with an introduction to the basic concepts and generally succeeding in indicating its scope and depth. The selected references given at the end of each chapter provide a useful introduction to some more detailed sources of information.

The book centres around an excellent chapter "Food processing and preservation" which summarises the diverse techniques used and explains the scientific basis of each. Examples are taken from commercially available products to illustrate these preservation techniques and to explain some of the technological problems encountered with each.

The book starts with a brief history of the development of food processing and then summarises the world food situation, emphasising the important role that food technology will have to play in resolving the world food crisis. There is then a chapter on food quality and its assessment (surprisingly the least successful in my opinion) followed by a survey of human nutrition which includes a section on the effects of raw material handling, processing and storage on the nutritive value of food.

After the chapter on food processing and preservation there are shorter chapters on packaging, safety and sanitation (which includes water supply and effluent treatment), food laws and careers in food science and technology. These last two chapters refer mainly to the United States but still make worthwhile reading for the British student.

Almost all foods are manufactured from natural products and consequently all workers in the field (both scientists

terms with the variability of their raw material. To do this it is essential that they have some knowledge of statistics and agriculture and for this reason I regret that the authors chose not to include a chapter on either subject. Perhaps the inclusion of two further chapters would have increased the cost beyond the means of the "prospective food scientists and technologists" for whom it was written.

The authors must be congratulated on condensing so much of the essence of food science into this book and on maintaining a comprehensible and readable style throughout. It would be a useful addition to the bookshelf of any student of food science as well as to that of graduates of other disciplines starting work in the field.

JOHN WOODMAN

Ethylene in Plants

Ethylene in Plant Biology. By Frederick B. Abeles. Pp. xii+302. (Academic: New York and London, June 1973.) \$18.50.

THERE was a time when auxin was invoked as the master controller of all plant growth and developmental processes. It now seems that ethylene, whose dramatic effects on plants have been known for more than 70 years, is rapidly slipping into that role. In the past 10 years there has been a veritable explosion of research into the physiological actions of ethylene directed towards assessing its significance as a 'natural' hormone.

Dr Abeles has made a thorough survey of the bulky and confusing literature on this topic from the earliest indications of ethylene damage to plants over a century ago to the most recent and sophisticated biochemical and physiological studies. The topics covered are far ranging and include such matters as the practical use of ethylene and related compounds in plant production, the part played by ethylene as an air pollutant, its chemistry and analytical techniques for its estimation. Anybody interested in plant hormones and the chemical control of plant growth and development will find this a mine of information and references.

Having read the book from cover to cover, however, the reader will still be in doubt as to the importance and significance of ethylene as an endogenous growth regulator. Ethylene seems to do everything, but inconsistently, and all this is reported thoroughly and fairly. Although Dr Abeles is clearly a believer in ethylene as a major plant hormone, he has been unable to weave from this tangle of the literature a logical story to convince the sceptic. But he should not be criticised on this score; the time honoured auxin saga is no clearer.

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CORRESPONDENCE

Smoking in Pregnancy

SIR,—It seems likely that smokers, in general, lead a markedly different life-style from non-smokers, and that the life-style of the smoking mother during pregnancy may be less supportive of the developing foetus. So it is proper to be cautious in interpreting the association between maternal smoking and perinatal death.

In this context, Professor Burch (*Nature*, 245, 277; 1973) notes the evidence, and it is strong, that the low-birth-weight babies of smoking mothers are healthier than those of non-smokers. He seems to suggest that this, too, is evidence against the hypothesis that maternal smoking causes perinatal deaths. Is it not more reasonable to interpret it as merely evidence that maternal smoking is not so harmful to the infant as other causes of low birth weight? In general these causes are very powerfully associated with perinatal death: infants weighing 2,500 g and less at birth are sixteen times more likely to suffer perinatal death than those weighing more than 2,500 g (ref. 1).

Suppose that maternal cigarette smoking causes a weight loss of 5% in each baby: and suppose that each such baby has a 25% greater chance of suffering perinatal death than it would have if the mother had not smoked. Then consider that class of babies weighing less than 2,500 g and born to smoking mothers. About half of them are in that class for no reason other than that, having been born to smokers,

their weight has been reduced, thus transferring them from the heavier class to the lighter one. *Ex hypothesi*, their probability of perinatal death is 25% greater than it would have been if their mother had not smoked. But it is far less than that of the other babies in that class—those who would have been in that class whether their mothers had smoked or not.

In short, the effect of smoking is to augment that class with some relatively healthy babies. So it seems to me that the observed interaction between maternal smoking and birth weight, far from being mysterious, is exactly what would have been expected on the hypothesis that, besides depressing birth weight, maternal smoking has a rather weak causal association with perinatal death.

One would expect a similar interaction between birth weight and any factor if that factor both depressed birth weight and slightly increased the probability of perinatal death.

Let us consider social class, twinning and race. Babies of low social class have higher perinatal mortality rates and lower birth weights than babies in the upper social classes. For weights greater than 3,000 g there is a steady increase in perinatal mortality as social class declines. In the weight class 2,501 to 3,000 g, however, there is a steady decline in mortality rate as social class declines. And in the weight classes less than 2,500 g, there is further evidence that babies born to upper-class mothers are not the healthiest².

Twins have higher perinatal mortality

rates and lower mean birth weights than singletons. However, low-birth-weight twins have a better chance of survival than low-birth-weight singletons³⁻⁶.

In the United States non-white babies have lower mean birth weights and a higher perinatal mortality rate than whites. Nevertheless, among low-birth-weight babies, the non-whites have lower neonatal mortality rates than the whites⁷. In regard to stillbirth rates there is also an interaction (Table 1).

Each of these interactions, viewed in isolation, may be perplexing at first sight. But when seen in conjunction with others, there seems a common-sense explanation behind all of them. I suggest that it applies to maternal cigarette smoking too.

Yours faithfully,

WILLIAM H. JAMES

The Galton Laboratory,
Department of Human Genetics and
Biometry,
University College London

- ¹ Butler, N. R., and Bonham, D. G., *Perinatal Mortality*, 133 (Livingstone, London, 1963).
- ² Butler, N. R., and Bonham, D. G., *Perinatal Mortality*, 139 (Livingstone, London, 1963).
- ³ Ferguson, W. F., *Obstet. Gynec., N.Y.*, 23, 861 (1964).
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- ⁵ Gittelsohn, A. M., and Milham, S., *Br. J. prev. soc. Med.*, 19, 8 (1965).
- ⁶ Butler, N. R., and Alberman, E. D., *Perinatal Problems*, 133 (Livingstone, London, 1969).
- ⁷ Shapiro, S., Schlesinger, E. R., and Nesbitt, R. E. L., *Infant and Perinatal Mortality in the U.S.: National Center for Health Statistics, Series 3*, 4, 21 (United States Department of Health, Education and Welfare, Washington, DC, 1965).
- ⁸ *Vital Statistics of the United States for 1963, Natality*, 1 (United States Department of Health, Education and Welfare, Washington, DC, 1964).
- ⁹ *ibid.*, *Mortality*, 2, A (1965).

Table 1 Stillbirths (Late Foetal Deaths)/Live Births by Birth Weight and Colour*

	Birth weight (g)								
	1,000 or less	1,001–	1,501–	2,000–	2,501–	3,001–	3,501–	4,001–	4,501–5,000
White	0.655	0.251	0.103	0.030	0.008	0.004	0.003	0.004	0.011
Non-white	0.620	0.264	0.107	0.035	0.010	0.006	0.007	0.013	0.030

* Calculated from official United States data^{8,9}.

Obituary

Professor E. A. Stewardson

PROFESSOR E. A. STEWARDSON, Emeritus Professor of Physics, Leicester University, who died on August 24, 1973, at the age of 68, was born in 1904, and educated at Hawarden County School, North Wales. He graduated from the University of Liverpool in 1924 with first class honours in physics

and took his MSc in 1925. After holding appointments at the University of Liverpool and the National Central University, Chungking, he came to Leicester University College in 1940 and became the first Professor of Physics in 1946. He retired in 1969.

Professor Stewardson's main interest was what nowadays would be called 'atomic physics' rather than 'modern

physics' and a great deal of his research was spent on soft X-ray spectroscopy. Over the years he developed considerable experimental expertise in this field and this was to prove a valuable asset in the latter part of his scientific career.

Professor Stewardson was also a keen amateur astronomer and when, in the late 1950s, it was decided that part of the UK space research programme

should be to investigate the soft X-ray emission of the Sun, it was no surprise that Professor Stewardson's ability was called upon. A collaborative venture between the Universities of Leicester and London ensued, and in 1961 the first direct spectral data for solar soft X-rays were obtained by mounting a soft X-ray spectrometer on a rocket. During the next few years a group devoted to the soft X-ray side of space physics was set up under the direction of Professor Stewardson at the University of Leicester. Some of the successful joint experiments were those on an orbiting solar observatory in 1967 and 1968 and the recently acclaimed X-ray telescope array.

In parallel with the space application of soft X-ray spectroscopy, Professor Stewardson maintained a strong interest in other aspects of atomic physics. He was interested in electron-nuclear collisions and supervised the building and operation of a van de Graaff accelerator in Leicester in the early 1950s.

He will be missed by his colleagues and friends at Leicester.

Announcements

Appointments

THE following have been appointed members and officers of the **International Office of Radiological Protection** for 1973-77. Chairman, **Dr C. G. Stewart** (Canada), **Professor B. Lindell** (Sweden), **Dr D. J. Beninson** (Argentina), **Dr H. Jammet** (France), **Dr J. Liniecki** (Poland), **Dr A. S. McLean** (Great Britain), **Professor Y. I. Moskalev** (USSR), **Dr H. B. Newcombe** (Canada), **Dr E. E. Pochin** (Great Britain), **Professor S.**

Takahashi (Japan), **Professor A. C. Upton** (USA), **Dr J. Vennart** (Great Britain), **Professor Sir Brian Windeyer** (Great Britain). Members Emeritus, **Professor K. Z. Morgan** (USA) and **Dr L. S. Taylor** (USA). Scientific Secretary, **Dr F. D. Sowerby** (Canada).

Professor Francis O'Grady, University of London, has been appointed to the Foundation Chair of Microbiology, University of Nottingham.

The following have been appointed members of the Natural Environment Research Council: **Professor F. G. T. Holliday**, **Professor A. W. Skempton**, **Dr R. G. West**, **Dr I. Maddock**, and **Mr D. J. Lyons**.

Dr K. Hellmann of the Cancer Chemotherapy Unit, Imperial Cancer Research Fund, has been appointed Visiting Professor of Cancer Chemotherapy to the Westminster Medical School, University of London.

Errata

IN the bibliography of the book *Notes on the History of Nutrition Research* (reviewed *Nature*, 245, 442; 1973) the publisher and prices should have read: (Huber: Stuttgart, Berne and Vienna, 1973.) 42 Sw. fr.; 38 DM.

IN the article "Model for the Mating Protocol of Synchronously Flashing Fireflies" by J. E. Lloyd (*Nature*, 245, 268; 1973) paragraph 11, line 7 and following, should read "This is not apparent and perhaps does not occur in most *Pteroptyx* species. I spent many hours within swarms watching individuals and once saw this: a male received a luminescent response to his signals from a female 30 cm away and walked to her and mounted her immediately".

International Meetings

December 3, **The Bragg Lecture** (Dr H. Judith Milledge, Secretary, Bragg Lecture Fund Committee, Chemistry Department, University College London, Gower Street, London WC1).

December 17-21, **Marine Waste Disposal and Marine Pollution** (Istituto di Ingegneria Sanitaria del Politecnico di Milano, Segreteria per i Convegni Internazionali, Piazza Leonardo da Vinci 32, 20133 Milan).

December 18, **Second Scottish Perkin Symposium** (Professor P. L. Parson, Department of Pure and Applied Chemistry, University of Strathclyde, Cathedral Street, Glasgow G1 1XL).

December 18-19, **545th Biochemical Society Meeting** (Meetings Officer, The Biochemical Society, 7, Warwick Court, Holborn, London WC1R 5DP).

Reports and Publications

not included in the Monthly Books Supplement
Great Britain and Ireland

Clean Air Council. Working Party on the Publication of Information about Industrial Emissions to Atmosphere. Pp. 29. (London: Department of the Environment (Room 541), 28 Broadway, SW1, 1973.) [107]

Agricultural Research Council. Letcombe Laboratory—Annual Report for 1972. Pp. ix+69. (London: Agricultural Research Council, 1973. Obtainable from HMSO.) 85p. [107]

University of Oxford. Annual Report of the Curators of the Bodleian Library for 1971/1972. Pp. 61. (Supplement No. 6 to the *University Gazette*, Vol. CIII, June 1973.) (London: The University, 1973.) £1. [107]

Energy World, No. 1, July 1973. (Bulletin of the Institute of Fuel.) Pp. 1-32. (London: The Institute of Fuel, 1973.) [107]

Element Cards: a Games Approach to Mastery of the Chemical Elements. By Joseph Lipson. £2.40; DM 20. Teacher's Guide. Pp. 96. £1.25; DM 10.50. (London: Heyden and Son, Ltd.; Rheine/Westf.: Heyden and Son, GmbH., 1973.) [107]

The Zoological Record. 1968, Vol. 105, Section 20: List of New Generic and Subgeneric Names Recorded in Volume 105. Compiled by H. O. Ricketts. Pp. 18. 1969, Vol. 106, Section 13: Insecta. Compiled by the Staff of the Zoological Society of London. Pp. xii+589. £12; \$29. (London: The Zoological Society of London, 1973.) [107]

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(1712)

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Applications, with curriculum vitae and names of three referees, should be sent to J. Cunningham, Professor of Physical Chemistry, and should arrive before December 14, 1973.

(1671)

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Yearly Salary:

- (a) \$A6,012 minimum; \$A8,981 maximum.
- (b) \$A9,151 minimum; \$A10,674 maximum.

Note: Generally appointment will be within the salary range (a) according to qualifications and experience but applicants possessing special qualifications or extensive experience may be considered for appointment to salary range (b).

Duties: Investigations into the quantitative ecology of Port Phillip Bay with a view to assessing the effects of industrial and domestic development on the area; other duties as directed.

Qualifications: An approved degree in Science with Botany as a major. Appropriate training and experience in marine ecology with special emphasis on primary productivity as related to macrophytes is desirable.

Applications, quoting reference number (J/01), should be addressed to the Secretary, Public Service Board of Victoria, State Public Offices, No. 1 Treasury Place, Melbourne, 3002, Australia, by not later than 9.30 a.m. on Wednesday, 12th December, 1973, together with statements of experience and qualifications and date and place of birth.

(1668)

ULSTER:
THE NEW UNIVERSITY

SCHOOL OF BIOLOGICAL AND
ENVIRONMENTAL STUDIES

RESEARCH
ASSISTANT

Applications are invited for a Postdoctoral Research Assistantship for work on the bottom fauna of Lough Neagh.

The appointment will be for three years commencing on January 1, 1974.

Commencing salary (with F.S.S.U.): £1,929.

Further particulars should be obtained from: The Registrar, The New University of Ulster, Coleraine, Co. Londonderry (quoting Ref.: 73/141) to whom applications, including the names and addresses of two referees, should be sent not later than December 7, 1973. (1696)

UNIVERSITY OF SHEFFIELD
DEPARTMENT OF HUMAN BIOLOGY
AND ANATOMY

TISSUE CULTURE
TECHNICIAN

(GRADE 5)

Applicants with good practical knowledge of tissue culture, organ culture and similar methods essential. Minimum qualification: H.N.C. or equivalent.

Salary scale £2,007 by £75 (5) to £2,382 per annum. The working conditions and surroundings are pleasant, 37½-hour week, with excellent holidays and other conditions of service.

Please write to Professor R. Barer, Department of Human Biology and Anatomy, The University, Sheffield S10 2TN, to whom informal enquiries may also be made. (Ref. B.51/0). (1689)

MEDICAL RESEARCH COUNCIL

Pneumoconiosis Unit

BIOLOGIST

Junior Technical Officer required to assist in cell studies in asbestos cancers. Tissue culture experience preferred. Qualifications required: University degree, Higher National Certificate or equivalent. Scientific staff appointment considered for suitably qualified graduate (First or Upper Second Class Honours).

Apply giving details of age, qualifications, experience, and the names of two referees to: The Director, M.R.C. Pneumoconiosis Unit, Llandough Hospital, Penarth, Glam. CF6 1XW. (1655)

UNIVERSITY OF NEW SOUTH WALES
PROFESSOR OF FOOD TECHNOLOGY

Applications are invited for appointment to the above-mentioned chair in the School of Chemical Engineering. The present Head of School is Professor R. T. Fowler. Applicants should be experienced in food science and technology and be capable of providing leadership in their particular fields of interest. Professional qualifications and research experience in areas such as chemistry, biochemistry, microbiology or nutritional standards of foods are desirable. The professor will supervise and participate in teaching and examining undergraduate and postgraduate students in the School and engage in and promote research and advanced study in the field of his chair.

The successful applicant will become the head of the Department of Food Technology. Establishment of the department in the future as a separate school is being considered.

Salary \$A19,102 per annum. Subject to the consent of the University Council, professors may undertake a limited amount of higher consultative work. The University reserves the right to fill any chair by invitation.

Applications close in Australia and London on March 1, 1974.

Details of appointment, including superannuation, study leave and housing scheme, may be obtained from the Association of Commonwealth Universities (A.C.U.), 36 Gordon Square, London WC1H 0PF.



Imperial
Chemical
Industries
Limited

Industrial Hygiene
Research Laboratories

Senior
Toxicologist

The Laboratories are responsible for the safety evaluation of a very wide range of chemicals produced by ICI Limited. The Acute Toxicity Unit has a key role in this work and, in addition to research and industrial hygiene interests, its activities include an extensive programme of toxicological testing. We are looking for a person to direct this programme. The successful applicant will probably be a first or second degree graduate in physiology or pharmacology with several years experience in a field relevant to the Unit's activities.

Applicants should be people wanting to have a wide-ranging remit involving them in a variety of activities with both scientific and commercial facets, and who have the ability to motivate people and organise team activities.

An attractive salary will be offered to the successful applicant.

Applications and enquiries to:

Miss A Waring
Personnel Officer
ICI Limited
Industrial Hygiene Research Labs
Alderley Park
Nr. Macclesfield, Cheshire SK10 4TJ
Tel: Alderley Edge 2711 ext. 156

(1724)

Ministry of Defence
Microbiological Research Establishment,
Porton Down.

Microbiologist

■ Work on growth of micro-organisms ■ Develop seed production and culture methods to optimise yield of microbial products required for research ■ Products under investigation include therapeutic enzymes, and macromolecules such as tRNA and tRNA synthetases.

□ Degree/HNC in Microbiology, Applied Biology or Biochemistry □ Age under 27 □ Appointment as Scientific Officer (£1318-£2177) □ Ref: SA/2/FQ □ Closing date 14 December, 1973.

□ Application forms from Procurement Executive, Ministry of Defence, SPM1b3, Savoy Hill House, Savoy Hill, London WC2R 0BX, telephone 01-836 1207 ext 1625 or 1667.

(1690)



IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

Department of Mathematics

Lectureship in Numerical Analysis

A Lectureship in Numerical Analysis is vacant at a salary on the scale £1929 × 129–2058 × 165–4368 × 180–4548 per annum, plus London allowance of £162 per annum.

Candidates should have research interest in the mathematical analysis of numerical methods in one of the following areas: Linear Algebra, Non-Linear Equations, Integral and Differential Equations, approximation theory or optimization. Practical computer experience in the subject is an advantage. Lecturing duties involve teaching to postgraduate students, to undergraduate students in the Department of Mathematics, and to students of other departments.

Applications or enquiries about the post should reach Professor D. R. Cox, Department of Mathematics, Imperial College, London SW7 2RH, by Monday, 3rd December 1973. Applications should name three referees.

(1698)

YORKSHIRE WATER AUTHORITY Director of Scientific Services

Applications are invited for this post from persons now employed in the water industry as defined in Circular 5/73 of the Water Services Staff Commission.

The Authority is responsible for the integration of water supply, sewerage and sewage disposal, and river management services in the region to secure the optimum use of water resources. It will become a large business enterprise with an extensive capital investment programme and a large technically qualified staff.

The Director of Scientific Services will be a member of the management team and will be located in the head office of the Authority in Leeds. He will be primarily responsible for the scientific leadership of the work of the Authority and for the scientific content of advice and reports dealing with the whole of the Authority's operations. He will be responsible for the control of scientific research and development throughout the Authority and for the coordination of all laboratory functions. He will have, under his direct control, the operation of the central laboratory in Leeds. He will also be responsible for maintaining an independent quality control service for water supplies, effluents and rivers, and for the scientific content of the work of the Fisheries Officer.

The salary, which will be commensurate with the importance of the post, is under discussion with the Pay Board.

Detailed applications should reach the Acting Personnel Officer, at the address below by 7th December, 1973.

J. C. BROWN
Chairman

Yorkshire Water Authority,
21 Park Square South,
LEEDS LS1 2QG.

(1695)

MASSEY UNIVERSITY PALMERSTON NORTH, NEW ZEALAND LECTURER/SENIOR LECTURER IN FOOD PROCESSING

Applications are invited for the above-mentioned position in the Department of Food Technology. Applicants should be suitably qualified in Food Science, Technology or Engineering and have had experience in the food industry or applied food research. It is important that the applicant have a strong quantitative approach to processing.

The major commitment of the appointee will be in teaching Food Processing to undergraduate and postgraduate students taking the Food Technology option of the Technology Degree. He will be encouraged to develop liaison with one or more sectors of the food processing industry, and to develop an appropriate research area.

Appointment will be on the Lecturer/Senior Lecturer scale according to qualifications and experience.

Salary: Senior Lecturer, NZ\$8,249 to NZ\$9,723 to NZ\$10,606; Lecturer, NZ\$6,335 to NZ\$8,103.

Further details of the position and of the University together with general conditions of appointment, may be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF, or from the Registrar of the University.

Applications close on January 5, 1974. (1680)

HAREFIELD HOSPITAL HAREFIELD, MIDDLESEX

STUDENT, TECHNICIAN OR CARDIOGRAPHER required for training as technician. Modern department in Regional Cardio-Thoracic Centre. Day release for O.N.C. and practical training in all aspects of cardiac investigations, cardio-surgical and intensive care monitoring, paediatric investigations, surgery and pacing techniques. The Department works a 38-hour week, hours to be arranged by interview. Single accommodation can be provided.

SENIOR PHYSIOLOGICAL MEASUREMENT TECHNICIAN (CARDIOLOGY). Physiology graduates or O.N.C., H.N.C. qualified, or experienced physiological technician required to act as Deputy to Chief Technician. Responsibilities include some administration and training of junior staff. Duties include theatre monitoring, routine investigations of adults and paediatric patients, and pacing service with follow-up clinics. Single accommodation can be offered if needed.

Applications should be made to Hospital Secretary giving age, experience and names of two referees. Job descriptions can be obtained by telephoning Harefield 3737, ext. 3 or 179. (1702)

THE NEW SOUTH WALES INSTITUTE OF TECHNOLOGY SYDNEY, AUSTRALIA

The New South Wales Institute of Technology is a corporate institution for higher education established to provide a wide range of professional courses for those entering or already employed in industry, government and technological fields. The Institute, which is a degree awarding body, is currently undertaking a major building programme on a central city site in Sydney. Modern facilities are available including a well developed computer centre with remote terminals.

Applications are invited for appointment to the following two positions:

PRINCIPAL LECTURER IN PHYSICS (Ref. 73/282)

SENIOR LECTURER IN PHYSICS (Ref. 73/283)

One position is for a Theoretical Solid State Physicist with an interest in any of the following: Statistical Mechanics, Amorphous Semiconductors, Transport Properties of Non-metallic Materials, Diffraction Theory, Applied Mathematics.

The other position is for an Applied Physicist interested in Electronics, Solid State Devices, Optics (including Electron Optics), Materials Physics, Computer Control of Processes.

It is not specified which position is in which field. Applicants in either of the above areas should indicate if they wish to be considered at one of these levels or both.

Current research interests of the Department include Solar Power, Dilute Magnetic Systems, Transport Properties of Ceramic Materials, Neutron and X-Ray Diffraction.

Conditions.—Both positions carry tenure. Suitable provision is made for superannuation and long service leave and a housing loan scheme is available. Fares and a contribution towards removal expenses for the appointee and his family are provided. The Council of the Institute permits academic staff to undertake consulting for industry and government. Applicants should be prepared to commence at the Institute about the middle of 1974.

Salaries: Principal Lecturer, \$A15,308 to \$A15,940 per annum; Senior Lecturer, \$A12,268 to \$A14,308 per annum.

Applications close on December 15, 1973. Interviews will be held in London in early February, 1974.

Further information may be obtained from and applications should be addressed to: The Agent General for New South Wales, New South Wales.

Tropical Agriculture

Group Leader - International Consultancy - London

Bookers Agricultural and Technical Services provide a wide range of agricultural, technical and management services for sugar and other tropical and sub-tropical projects around the world. The Booker Group has assets exceeding £60 million and employs some 30,000 people.

A first-class tropical agriculturalist is now required to take charge of the non-sugar aspects of the company's consultancy. Reporting to the Agricultural Director he will be required to:

- co-ordinate the work of an expanding team of agriculturalists
- synthesise the contributions made by the individual members of each assignment team so as to ensure that a balanced report is submitted to the client



**BOOKER
McCONNELL**

- contribute his own skills to major consultancies as and when required.

Candidates, ideally aged 35-50, should be well qualified academically and have significant experience in tropical agriculture. They must be familiar with the principal tropical crops and be able to develop effective systems of agriculture, including the relevant inputs and outputs, under a wide range of ecological conditions. An appreciation of agricultural economics is particularly important. A willingness to travel overseas and the ability to work successfully with a variety of clients are essential.

An attractive salary, appropriate to qualifications and experience, will reflect the importance the company attaches to this senior appointment. Fringe benefits include an excellent pension, car loan scheme and, where appropriate, re-location expenses.

Please send brief career and personal details in the first instance to: E. C. Robinson,
Personnel Director,
Agricultural Division,
Booker McConnell Ltd.,
83 Cannon Street,
London EC4N 8EJ.

(1711)

May & Baker Ltd Physiologists/Pharmacologists

Applications are invited from graduate pharmacologists or physiologists interested in a career in the development of new therapeutic agents for the following posts:

Post-Doctoral Research Scientist for work with a team engaged in the study and development of new anti-asthmatic agents including prostaglandin-like drugs. Recent developments are most interesting and the work should have great appeal for a good research-orientated scientist interested in seeing a practical outcome to his work.

Post-Doctoral Research Scientist for work on gastric secretion. To develop and extend work of considerable promise already in progress leading to a new agent for the treatment of gastric and duodenal ulcers.

A Research Assistant with a good first degree together with some experience in drug research for work with a team involved in the study of new drugs for the treatment of coronary heart disease and atherosclerosis. Work of considerable interest is already in progress.

The research facilities provided by the May & Baker Research Institute are recognised as excellent. Team work is encouraged, as is publication in scientific journals and attendance at meetings of scientific societies.

May & Baker provide first-class conditions of employment including a highly competitive starting salary and contributory pension scheme with free life assurance cover.

Assistance towards removal expenses may be considered in suitable cases. Please apply in writing with details of qualifications and experience to The Personnel Manager, May & Baker Ltd., Dagenham, Essex RM10 7XS, quoting reference number 292/N/73.



M&B May & Baker

(1572)

GOVERNMENT OF SEYCHELLES

SENIOR CONSERVATION OFFICER

required as Head of the Forestry and Nature Conservation Division in the Department of Agriculture. He will be the chief executive officer of the National Park and Nature Conservancy Commission and will be its principal adviser. Male candidates only, MUST have experience in administration of natural resources, preferably tropical forestry, and proven practical ability in organising staff and activities in wild life management. A degree in Biology is desirable.

Commencing salary including Supplement will be approximately £4,160 a year. A substantial Gratuity is payable on completion of engagement which is for one tour of two to three years initially.

Because of lower rates of income tax in the Seychelles the gross emoluments are roughly equal to U.K. salaries of

£6,250 for a single man

£6,500 for a married man with two children

Other benefits include free passages, liberal leave on full salary, generous education allowances, and Government quarters at moderate rental. Appointment Grant up to £200, Car Advance £600 and Outfit Allowance £40 may be payable.

The post described is partly financed by Britain's programme of aid to the developing countries administered by the Overseas Development Administration of the Foreign and Commonwealth Office.

For further particulars you should apply, giving brief details of experience to:

crown agents

M Division, 4 Millbank, London SW1P 3JD, quoting reference number M3F/730929/NF.

(1662)

WELSH NATIONAL SCHOOL OF MEDICINE

(UNIVERSITY OF WALES)

Applications are invited for a

RESEARCH ASSISTANT

to carry out a fundamental investigation of the factors which determine the bonding of polymer films to tooth surfaces and their effectiveness in preventing mineral loss. Applicants should have a degree in Physics or Chemistry and be interested in the behaviour of polymeric systems. A wide range of physical instrumentation exists for examining the diffusion of ions through polymer films. Other supporting techniques are available in the Dental School and the Chemistry Department, who are jointly responsible for the project. The successful applicant will be expected to register for a higher research degree. The appointment will be for three years on an M.R.C. grant, salary £1,150 to £1,300. Further details and application forms can be obtained from the Registrar, The Welsh National School of Medicine, Heath Park, Cardiff CF4 4XN, and should be returned by December 31, 1973.

(1697)

GRADUATE OR POSTDOCTORAL RESEARCH ASSISTANT

required for one year in the first instance, to work in the Department of Microbiology under the direction of Professor C. A. Mims on the pathogenesis of murine cytomegalovirus infection. Some postgraduate experience in virology and tissue culture desirable.

Initial salary in the range £1,569 to £2,550 according to qualifications and experience.

Applications, together with the names of two referees, to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, by December 15.

(1593)

MARINE AQUATIST AND REPTILE KEEPER

LOCATION: MAJORCA

required for a subsidiary of a U.K. public company. Applicants should be preferably single and previous experience in a similar position is essential. Attractive conditions, salary negotiable.

Applications in writing to:

**D. Mudge, Esq., Pleasurama Ltd.,
7 Welbeck Street, London W1M 7PB.**

U.M.I.S.T.

JUNIOR PROGRAMMER/ PROGRAMMER

Applications are invited for a post of Junior Programmer or Programmer in the Department of Chemical Engineering.

In connection with an SRC project on Distillation and Absorption the Department has recently acquired a DEC PDP-11/40 computer for on-line plant data acquisition and control. The successful candidate will be required to assist in the development of operating systems and application programming for a variety of research projects.

Minimum requirements for this post are: a degree in engineering or science with at least one year's experience in assembly language and FORTRAN IV programming, preferably in real time applications. Candidates with lower academic qualifications who have obtained extensive programming experience will also be considered. The appointment is for a period of two years and will carry F.S.S.U. benefits.

Salary appropriate to qualifications and experience—in the range £1,569 to £2,271, with superannuation under the F.S.S.U.

Requests for application forms and conditions of appointment, quoting reference number CE/454, should be sent to the Registrar, The University of Manchester Institute of Science and Technology, Sackville Street, Manchester M60 1QD, to whom completed forms should be returned by December 3, 1973. (1648)

MEDICAL RESEARCH COUNCIL BLOOD PRESSURE UNIT GLASGOW

GRADUATE BIOCHEMIST/CHEMIST

capable of working relatively independently, is required to work in the peptide laboratory of the above Unit, at the Western Infirmary, Glasgow. Among other things the work will involve the development of techniques for the separation and estimation of plasma vasoactive peptides (angiotensin and vasopressin) and their breakdown fragments, and the application of these methods in various physiological and haemodynamic situations.

Applications to the Unit Secretary; further details can be obtained from Dr. J. J. Morton in the Unit (041-339 3124).

(1656)

UNIVERSITY OF CAMBRIDGE SIR WILLIAM DUNN READERSHIP IN BIOCHEMISTRY NOTICE

The Appointing Committee for the Sir William Dunn Readership in Biochemistry invite applications for appointment to this Readership in the Department of Biochemistry from March 1, 1974, or a later date to be arranged. The appointment will be subject to the Statutes and Ordinances of the University and will be to the retiring age.

The pensionable stipend of a Reader who is not ordinarily resident in College is £5,247 a year, or £5,148 a year if the Reader is ordinarily resident in College. The stipend would be subject to a deduction if the Reader is a Fellow with dividend or Head of a College. A Reader is not allowed to be a Tutor, Assistant Tutor, Bursar, Assistant Bursar, or Steward of a College, nor to give instruction on behalf of a College or Colleges for more than six hours a week.

Information about the reimbursement of removal expenses and, for persons resident outside the United Kingdom, travelling expenses may be obtained from the Secretary of the Appointing Committee.

A candidate should send twelve copies of his application, together with the names of not more than three referees, to Mr G. R. Anderson, Secretary of the Appointments Committee of the Faculty of Biology 'B', General Board Office, The Old Schools, Cambridge CB2 1TT, so as to reach him not later than December 31, 1973.

(1678)

ST. BARTHOLOMEW'S HOSPITAL LONDON E.C.1

PHYSICIST for the clinical Radio-Isotope Department to work on project involving computer analysis of brain-scans. Applicants should be graduates, preferably first or second class honours. Previous experience of brain-scanning techniques not essential. Salary in the range of £1,278 to £1,980 plus London Weighting according to qualifications and experience.

**ROTHAMSTED EXPERIMENTAL
STATION**
HARPENDEN, HERTS AL5 2QJ
SCIENTIFIC OFFICER

required in the Molecular Structures Department for X-ray diffraction studies by photographic and counter methods. Responsibilities will include care and operation of equipment. Current experimental work includes structural chemistry of compounds of importance in agriculture, pesticides and complexes of alkali and of alkaline earth metals.

The Department is moving to Rothamsted from London early in 1974.

The appointment would be suitable for an applicant with HND or HNC in Physics, Electronics or Engineering, or an equivalent qualification.

Appointment in grade of Scientific Officer, £1,318 to £2,177. Starting salary according to qualifications and experience. Superannuation with allowance to offset contributions.

Applications, naming two referees and quoting reference 2022, to the Secretary by December 14, 1973. (1657)

UNIVERSITY OF NEW ENGLAND
ARMIDALE, NEW SOUTH WALES
**LECTURER/SENIOR
LECTURER IN
HORTICULTURAL AGRONOMY**

This is an appointment in the Department of Agronomy and Soil Science. The successful applicant will be required to teach and supervise post-graduate students in fields of horticulture and agronomy and should have experience in these general areas. Although academic quality is of prime importance some preference may be given to applicants with experience in one of the following fields—plant nutrition, plant (weed) ecology and crop (horticultural) physiology. It is hoped the appointee will take up duty on February 1, 1974.

In addition to laboratory, field station and glass-house facilities, modern growth cabinets are available for detailed controlled environmental studies, and special equipment exists for biochemical analysis, work with radiolabelled CO₂, gas analysis, measurement of soil water and other environmental parameters, and for specialised plant and soil analysis. Good opportunities exist for co-operative work with other departments within the Faculty of Rural Science and with the Department of Botany and Agricultural Economics, the School of Natural Resources and with the CSIRO Division of Animal Physiology.

Appointment can be made to the permanent staff but the University reserves the right to make the appointment probationary where it considers this appropriate.

Salary: Lecturer \$A8,698 to \$A11,982; Senior Lecturer \$A12,268 to \$A14,308 p.a.

Conditions include provision for travel and removal expenses. In addition, superannuation is available, together with assistance in buying or building a home. Study leave grants are available and credit may be granted for existing study leave entitlement.

Further information may be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF.

Applications close on December 7, 1973. (1709)

**OXFORD
POLYTECHNIC**

Applications are invited for the following post with effect from January 1, 1974.

**Lecturer II in Histology and/or
Comparative Animal Physiology**
(£2,525 to £3,243)

Further details and application forms from

The Head of Department of Science,
Oxford Polytechnic,
Oxford OX3 0BP.

**University of Zürich, Switzerland
Division of Cancer Research**

**Research Assistantship
in Experimental
Biology/Pathology**

immediately available in a team studying invasion and spread of cancer with methods of bio- and cytochemistry, cinemicrography and electron microscopy. Applicant will mainly work with various in vivo models of invasive growth.

Salary according to Swiss university standards. Knowledge of German not necessary.

Please apply to Abteilung für Krebsforschung, Aussenstation der Universität Zürich, Birchstrasse 95, 8050 Zürich, Switzerland. (1717)

**C. H. Boehringer Sohn
Ingelheim-am-Rhein
West Germany**

This International Company, which manufactures a wide range of pharmaceutical and allied products, has an immediate vacancy for a Histopathologist with a special interest in Toxicology. The post is at the research laboratories, situated at Ingelheim-am-Rhein near Frankfurt, and the work will involve histological evaluation of toxicity investigations in all species of laboratory animals. However, a proportion of working time will be set aside for the pursuit of any personal research which the appointee may wish to undertake.

The successful candidate will be within the age range 30-35 years, single or married, will hold a degree in Medicine from a British University, and will have had at least four years experience in the field of general pathology and histopathology, although previous involvement with experimental animal pathology is not essential. A knowledge of German would be advantageous but is not a prerequisite.

An attractive salary will be dependent on age and experience but will be fully commensurate with rates of remuneration in Germany. The appointee will be expected to take up residence in reasonable proximity to the Research Laboratories, and full assistance will be given to finding and moving to satisfactory accommodation.

Initial interview for this post will be in London. Please write in confidence to Dr. P. A. Knowlson, Medical Director, Boehringer Ingelheim Limited, Southern Industrial Estate, Bracknell, Berkshire, RG12 4YS.



**Boehringer
Ingelheim**



British Petroleum is expanding its oil and gas exploration programme throughout the world whilst continuing to develop existing production areas. The following Exploration personnel are required:

Geologists and Geophysicists

Though we will have vacancies at several levels of experience, we are particularly interested in men with a good academic background and 6 or more years of Oil of Oil Service Company experience, who are interested in a career that could take them to any part of the globe.

Geological Specialists

A **Micro-Palaeontologist** and a **Palynologist** for initial posting to our Research Centre at Sunbury-on-Thames but with the probability of assignments to Scotland or overseas in the future.

A **Petrologist** who will be attached to our North Sea Operations base at Aberdeen after an initial introductory period at the Research Centre at Sunbury-on-Thames.

Terms of service will be those expected from a U.K.-based major oil company. Consideration would be given to assistance with re-location expenses where appropriate.

■ Please, write giving brief details of age, qualifications and experience, quoting reference U.654, to: The Manager, Central Recruitment, The British Petroleum Company Limited, Britannic House, Moor Lane, London EC2Y 9BU.

(1659)

Reckitt & Colman

Neuropharmacological Research

This opportunity is for a graduate with 2 or 3 years experience in pharmacological research, at least part of which should ideally have been in the field of neuropharmacology. The successful applicant will be involved in fundamental investigations involving stereotactic and neurochemical techniques. The objectives of this long-term research project include the elucidation of the chemical basis of certain mental illnesses.

Reckitt & Colman operates internationally and its pharmaceutical interests are based at Hull where first class facilities are available. Over the next few years major investment is planned in an expansion of the Company's pharmaceutical research activities.

Salary is negotiable according to experience and qualifications. Fringe benefits include annual bonus and relocation assistance.

Please write quoting ref. U.52 and giving brief relevant details of experience and qualifications to: C. E. Rhodes, Pharmaceutical Division, Reckitt & Colman Ltd., Dansom Lane, Hull HU8 7DS.

UNIVERSITY COLLEGE OF
WALES
ABERYSTWYTH

Department of Agriculture

Applications are invited for the post of

FIELD ASSISTANT

Initial salary: £1,115 per annum.

The post is newly created and supported for up to five years by the Potato Marketing Board. Duties will involve helping with experimental work at Trefoyn Farm, Tenby, Pembrokeshire, including field work in growing the crops and also detailed recording throughout growth and storage. Ability to drive a tractor and experience in farm operations an advantage. The successful applicant will be expected to live in Pembrokeshire.

Application forms obtainable from the Registrar, to whom completed applications should be returned by December 7, 1973.

(1686)

MASSEY UNIVERSITY
PALMERSTON NORTH, NEW ZEALAND
SENIOR LECTURER/LECTURER
IN VETERINARY PUBLIC HEALTH
AND MEAT HYGIENE

Applications are invited from veterinary graduates for this new post in the Department of Veterinary Pathology and Public Health. Applicants should have an interest in meat hygiene and preferably experience in some aspects of veterinary public health. Although direct experience of meat hygiene is desirable, it is not essential.

The successful applicant will be required to assist in the teaching of veterinary public health and meat hygiene to both undergraduate and postgraduate students, and to develop research in appropriate fields of study.

This new position is part of a challenging new development within the Veterinary Faculty following the appointment of Professor D. K. Blackmore to the foundation chair of Veterinary Public Health and Meat Hygiene. The position involves close co-operation with workers in related disciplines, both within and outside Massey University.

Present salary scales are: Lecturer—NZ\$6,335-\$8,013; Senior Lecturer—NZ\$8,249-\$9,723 (bar)—NZ\$10,606.

Further details of the position and of the University, together with general conditions of appointment may be obtained from the Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF.

Applications close on January 31, 1974. (1710)

UNIVERSITY OF BIRMINGHAM
FACULTY OF MEDICINE AND DENTISTRY

Applications are invited for a TEMPORARY LECTURESHIP in the DEPARTMENT OF PHYSIOLOGY in the Medical School. Preference will be given to medically qualified applicants.

Salary in the scale £1,929 to £4,548 plus F.S.S.U. Applications (9 copies) naming three referees should be sent by December 14, 1973, to the Assistant Registrar, The Medical School, University of Birmingham, Birmingham B15 2TT. Further particulars may be obtained from the Head of the Department of Physiology, Professor S. M. Hilton.

(1646)

THE UNIVERSITY OF SHEFFIELD
ACADEMIC DIVISION OF MEDICINE

Applications are invited for a PRE- or POST-DOCTORAL RESEARCH ASSISTANT to join a group working with Professor D. S. Munro on human thyroid disorders. The work will include the development of new assay methods for circulating thyroid stimulating factors in health and disease. A graduate with a degree in Chemistry or in a biological science is sought. Experience in bioassay and radioimmunoassay is desirable but not essential. Salary up to £1,929 a year according to qualifications and experience. Further particulars from the Registrar and Secretary to whom applications (one copy), including the names and addresses of two referees,

MEDICAL RESEARCH COUNCIL**Toxicology Unit**

Applications are invited for a post in the Toxicology Unit to give technical assistance in biochemical investigations. Candidates with appropriate laboratory experience will be preferred. The appointment will be in the category of either Junior Technician/Technician or Junior Technical Officer. Salary and grade dependent on age, experience and qualifications.

Apply in writing only to the Director, Toxicology Unit, Medical Research Council Laboratories Woodmansterne Road, Carshalton, Surrey.

(1674)

**JAMES COOK UNIVERSITY OF
NORTH QUEENSLAND
LECTURERS¹ (2) IN ENGINEERING
(CIVIL)**

Applicants should possess a higher degree and have teaching and research experience in the fields of structural engineering (experience in research involving wind effects on buildings would be an advantage), or fluid dynamics and hydraulics (experience in fields of coastal engineering or sediment transport would be an advantage). The successful applicants will undertake teaching at undergraduate and postgraduate level, including supervision of laboratories, and will be expected to develop an active research programme in their fields of interest.

Salary range: \$A8,698-\$A11,982 p.a. plus locality allowance.

Conditions of appointment include FSSU superannuation, invalid pension scheme, housing assistance, study leave and allowance for travel and removal expenses on appointment.

Further details and application forms obtainable from the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close on December 14, 1973. (1721)

**UNIVERSITY OF
NEWCASTLE UPON TYNE
DEPARTMENT OF AGRICULTURAL
BIOCHEMISTRY**

Applications are invited for the post of Demonstrator in the Department of Agricultural Biochemistry. Persons applying should have an honours degree in Biochemistry, Agricultural Biochemistry or some related subject and have had postgraduate experience. Preference will be given to candidates with a research interest in biochemical mechanisms relating to domestic livestock. The post will be for three years subject to annual renewal.

The salary will be in the range £1,929 by £129 to £2,058 by £165 to £2,223 according to age, qualifications and experience. Membership of F.S.S.U. is required.

Applications should be submitted to Professor D. G. Armstrong, Department of Agricultural Biochemistry, Faculty of Agriculture, The University, Newcastle upon Tyne NE1 7RU, within three weeks of the appearance of the advertisement.

(1645)

**UNIVERSITY OF TORONTO
DEPARTMENT OF PHYSICS**

Applications are invited for a faculty position at the level of ASSISTANT PROFESSOR in the Department of Physics. Applicants should have a Ph.D. and research experience in solid earth physics. The solid earth physics group in the Department of Physics has an active and well supported research programme in geomagnetism, crustal seismology, tectonics and geochronology, and works in close co-operation with the Department of Geology. Appointment will be effective July 1, 1974.

Applicants should send curriculum vitae and names of three referees to: Professor D. J. Rowe, Department of Physics, University of Toronto, Toronto M5S 1A7, Ontario, Canada. (1439)

CAVENDISH MEDICAL CENTRE

A vacancy exists in the above Health Screening Centre for a CLINICAL BIOCHEMIST. This is an interesting post with good working conditions. Salary negotiable, commensurate with experience. Applications to Mrs Payne, '99 New Cavendish

The Board of Trustees for the
Netherlands Central Institute for Brain Research
in Amsterdam

invites applications for the position of:

DIRECTOR

of this Institute. The function will be open as of August 1, 1975.

This function carries with it the responsibility for the co-ordination and supervision of the research work of the Institute. Fundamental research is carried out in various disciplines concerning the nervous system. Contacts also exist with several clinical medical departments.

In addition, there is opportunity for carrying out one's own research interests.

Salary will be according to government civil service regulations. Further information can be obtained from: The Secretary of the Board of Trustees: Prof. P. E. Voorhoeve, Laboratory for Neurophysiology, Jan Swammerdam Institute, le Const. Huygensstraat 20 in Amsterdam (Holland).

Applications with curriculum vitae, list of publications and references should be sent within a month after publication of this advertisement to the same address. Information and recommendations concerning possible suitable candidates for this function are also welcome.

(1673)

Biochemists

A young enthusiastic biochemist is required to join a multi-disciplined research project team working in the area of the metabolic control of Obesity.

Experience in the field of lipid and/or carbohydrate intermediary metabolism is desirable but not essential.

There is also a similar vacancy in a feasibility study working on Growth Promotion.

Suitable candidates will probably be under 25 and have a B.Sc., M.I.Biol., HNC or HND in biochemistry or allied subject.

A good starting salary will be offered and reviewed regularly. There are generous fringe benefits including sick pay, non-contributory pension and a U.K. bonus scheme. The laboratories are situated in a pleasant area of Surrey within easy reach of London.

Please reply quoting Ref. W0 74 to the



**Personnel Officer,
Beecham Research Laboratories,
Walton Oaks,
Dorking Road,
Tadworth, Surrey.**

(1713)



1972

**MCGILL UNIVERSITY
DEPARTMENT OF BIOLOGY**

ECOLOGIST with research interests in freshwater zooplankton or benthos. Teaching duties will include a senior level course in environmental physiology of animals. Rank: Assistant Professor. Starting date: September 1974 or earlier.

Applicants should include curriculum vitae and the names of two or three referees. Write before February 1, 1974 to: Ms. E. Mader, Administrative Assistant, Department of Biology, McGill University, P.O. Box 6070, Station A, Montreal, Quebec, Canada

**THE UNIVERSITY OF MANCHESTER
RESEARCH FELLOW IN
CHEMISTRY**

Applications invited for this post (tenable for one year in the first instance) from holders of degrees in chemical physics or physics, for work on neutron scattering studies of polymers, in collaboration with A.E.R.E., Harwell, and I.L.L., Grenoble. Salary range per annum: £1,929 to £2,223.

Full applications, naming two referees, to Professor G. Allen, Department of Chemistry, The University

Technical Writer and Applications Specialist

A biochemist or cell biologist is required to join our Scientific Information and Service Department at our Headquarters in Uppsala, Sweden. We are an active group responsible for the preparation of scientific information material of all kinds. Laboratory testing of new products and applications work also form an important part of our work.

Our interests cover the whole field of biochemical separation methods and we are expanding rapidly in this and other fields.

Applicants should have research experience in biochemistry or cell biology, ideally in cryobiology. Clear and accurate expression in the written word is essential with English as the Mother Tongue.

Head of Technical Service

The fine Chemicals Division of Pharmacia (Great Britain) Limited manufacturers of Sephadex and other separation material require a graduate in biochemistry or in a biological science with chemistry, for our UK base. Experience involving customer contact will be useful.

Applicants must be able to evaluate and communicate scientific information at all levels. After initial orientation duties will include:

- ★ Answering verbal and written enquiries
- ★ Lecturing
- ★ Training Technical Sales personnel
- ★ Establishing and maintaining research contacts by attendance at scientific symposia
- ★ Assisting in the preparation of publicity material

The post offers a wide range of interests for the applicant with an enquiring mind; pleasant working conditions, life assurance, pension and other international company benefits.

Preferred age for both vacancies is 25-30. These are both important positions and will carry a salary commensurate with qualifications and experience.

Applications to:

Mr D. S. Sweetman
Sales Manager
Fine Chemicals Division
Pharmacia (Great Britain) Limited
Paramount House
75 Uxbridge Road
London W5 5SS



Pharmacia
Fine Chemicals

(1722)

THE OPEN UNIVERSITY

BIOLOGY TECHNICIAN (temporary post)

An immediate vacancy exists for a Biology Technician (Grade 2b) to assist in general laboratory work, care of animals, and the preparation of Open University teaching material in Biology. The appointment will be for one year in the first instance. Salary, based on qualifications and experience, will be within the Grade 2b scale £1,524-£1,794 p.a.

Further details and application forms are available from the Personnel Manager, The Open University (B2), Milton Keynes, MK7 6AL. (Tel. Milton Keynes 74066, Ext. 3068.) Closing date Monday December 3, 1973. (1704)

UNIVERSITY OF TORONTO ASSISTANT PROFESSOR IN BIOCHEMISTRY

Applications are invited for the position of Assistant Professor in the Department of Biochemistry, to take effect from July 1, 1974, or as soon thereafter as possible. The successful applicant will be required to take part in the teaching duties of the Department and develop his own research programme. The Department is involved in teaching undergraduates in the Faculties of Medicine, Dentistry, Arts and Science, and Nursing, as well as the Graduate School. The minimal salary for the position is \$14,300.

Applicants with suitable qualifications should send a curriculum vitae and the names and addresses of three referees, to Professor T. Hofmann, Department of Biochemistry, University of Toronto, Toronto, Canada M5S 1A8, to reach him not later than January 31, 1974. (1615)

ROWETT RESEARCH INSTITUTE BUCKSBURN, ABERDEEN, AB2 9SB SCIENTIFIC OFFICER

Applications are invited for a scientific post in the Department of Experimental Pathology. The successful candidate will be encouraged to undertake original work on toxic effects of dietary constituents in farm animals. A special interest in EM techniques and ultrastructural morphology, and ability to work with farm animals, are essential.

Salary scale is £1,318 per annum rising to £2,177 per annum. Candidates should have at least a good second class honours degree in science, and salary placing will be according to qualifications and post-graduate experience. The post is superannuated with a non-pensionable allowance to offset contributions.

Applications containing full biographical details and names and addresses of two referees, should reach the Secretary of the Institute before December 14. Further particulars of the duties of the post can be had on application. (1611)

UNIVERSITY OF NOTTINGHAM MEDICAL SCHOOL DEPARTMENT OF PHYSIOLOGY VACANCY FOR RESEARCH ASSISTANT IN CARDIOVASCULAR PHYSIOLOGY

Applications are invited from graduates for the post of Research Assistant to work on a research project concerned with the role of support hosiery in assisting venous function in the lower limbs. Graduates with a suitable background interested in this aspect of human biology are invited to write to Dr P. H. Fentem, Department of Physiology, Medical School, University of Nottingham, Nottingham NG7 2RD for further information and an application form which should be returned before December 14, 1973.

Initial salary will be within the scale £1,422 to £1,929 (with membership of F.S.S.U.) according to qualifications and experience. The appointment will be for two years. (1687)

TECHNICIAN required in Department of Botany, University of Reading, Whiteknights, to assist in research into the phytochemistry of higher plants, preferably with experience in analytical chemistry and/or chromatographic techniques and with appropriate H.N.C. or equivalent. Salary in scale £1,650 to £1,920 per annum (Grade 3). Apply with names of two referees, quoting Ref. T.N74, to Assistant Bursar (Personnel), University of Reading, Whiteknights.

ABSTRACTOR

Zoology graduate required as Abstractor for publishers of Aquatic Sciences & Fisheries Abstracts, Genetics Abstracts, Entomology Abstracts, Chemoreception Abstracts and Animal Behaviour Abstracts. Knowledge of French/German an advantage. Would suit recent graduate. N.U.J. salary scale. Apply Dr E. S. Krudy, Information Retrieval Limited, 1 Falconberg Court, London W1V 5FG. (1676)

UNIVERSITY OF SYDNEY
AUSTRALIA
LECTURESHIP/SENIOR
LECTURESHIP IN HISTOLOGY
AND EMBRYOLOGY

Applicants should have appropriate qualifications in Medicine, Dentistry, Veterinary Science or Science and research interests in Cytology, Histology or Embryology.

The position advertised is permanent but in appropriate cases an initial three-year appointment may be made with possibility thereafter of permanency or in certain cases return fares.

Salary range: Lecturer \$A8,698-\$A11,982 p.a.; Senior Lecturer \$A12,268-\$A14,308 p.a.

Applications, including curriculum vitae, list of publications and names of three referees by December 7, 1973, to the Registrar, University of Sydney, NSW 2006, Australia, from whom further particulars available. Information also available from Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF. (1708)

UNIVERSITY OF SYDNEY
AUSTRALIA
LECTURESHIP IN BIOLOGY

The appointment, which can commence in April 1974, will be in animal biology. Applications are particularly sought from persons with qualifications in invertebrate biology, marine biology or developmental biology.

The position advertised is permanent but in appropriate cases an initial three year appointment may be made with possibility of permanency thereafter or in certain cases return fares.

Salary range: \$A8,698-\$A11,982 p.a.

Applications, including curriculum vitae, list of publications and names of three referees, by December 14, 1973, to the Registrar, University of Sydney, NSW 2006, Australia, from whom further information is available. Information also available from Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF. (1720)

CHIEF TECHNICIAN

We have a vacancy in our Pharmacology Department for a Chief Technician. The man or woman appointed will co-ordinate a number of technical jobs related to the Department as a whole. He or she will also be responsible for certain Departmental facilities in the new Research Block.

We are looking for applicants with an H.N.C. or equivalent with several years' laboratory experience, though a Graduate may also be suitable for this position.

For information on the Company and an application form please apply by letter or phone to Mr N. Michell, quoting reference RD20/M.

ROCHE PRODUCTS LIMITED
 WELWYN GARDEN CITY,
 HERTFORDSHIRE AL7 3AY (1670)

NATIONAL VEGETABLE RESEARCH
STATION
AGRICULTURAL CHEMIST

There is a vacancy for an Agricultural Chemist in grade of Scientific Officer to join a small team modelling the effects of nutrient supply on plant growth. The applicant will be required to develop micro-techniques for inorganic analysis of plant sap, and to carry out experiments in the field and in glasshouses. Some work on commercial farms will also be involved.

Qualifications: degree, H.N.D., H.N.C. or equivalent in chemistry or in agricultural chemistry is required. Starting salary in scale £1,318 to £2,177 per annum according to qualifications and experience. Superannuation with allowance to offset contributions.

Full particulars and application form (to be returned by December 14, 1973) from the Secretary, N.V.R.S., Wellesbourne, Warwick. (1669)

RESEARCH AGRICULTURALIST required in Department of Agriculture and Horticulture for 3 years with possible extension to 5 years to undertake Research and Demonstration duties. Candidates should be Honours graduates in Agriculture or equivalent subject. The Research work which is expected to qualify the holder of the post for a higher degree, will be in Farm Management in relation to animal production. Salary £1,224-£1,503 p.a. over the five years.—Apply, quoting Ref. M.N77, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH (1714)



Imperial
Chemical
Industries
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Industrial Hygiene
Research Laboratories
Dust and Fibre
Toxicity

The Laboratories are expanding their programme of work on dust and fibre toxicity and need someone, with several years relevant post-graduate experience, to develop the techniques of assessing biological effect by both in vitro and in vivo methods, whilst continuing the ongoing work in the field of cytotoxicity.

This is a challenging position for a person who should have the originality and initiative to plan a long-term programme related to the needs of the Laboratories and integrated with relevant studies in other disciplines.

Applications to:

Miss A Waring
 Personnel Officer
 ICI Limited
 Industrial Hygiene Research Laboratories
 Alderley Park
 Nr Macclesfield Cheshire SK10 4TJ
 Tel: Alderley Edge 2711 ext 156

(1723)

UNIVERSITY OF DUNDEE
DEPARTMENT OF ANATOMY

Applications are invited for the post of

CHIEF TECHNICIAN

in the above department.

The post carries responsibility for the financial administration of the department and for the provision (with some ten other technical staff) of full technical service and assistance to the department's teaching and research staff, at present thirteen in number.

Candidates should preferably be aged 30 or over and have at least 10 years' relevant experience (not necessarily in an anatomy department) as well as formal qualifications to HNC level or equivalent. They should be competent in and willing to be personally involved in the provision of technical service (including the training of junior technicians) in one or more of the following areas—electron microscopy, histology, histochemistry, radioisotope techniques and associated electronic equipment, photography.

A suitably qualified candidate will be appointed at Technician Grade VII (salary scale £2,817 to £3,201). Appointment at a lower grade may be offered in the absence of suitably qualified applicants.

Applications, quoting Ref. EST/137/73J, containing the names and addresses of two referees and giving details of age, qualifications and experience, should be sent by December 10, 1973, to the Secretary, The University, Dundee DD1 4HN. Informal enquiries about the post may be made by telephone to Professor D. A. T. Dick, Dundee 23181, Ext. 547.

(1654)

ROYAL POSTGRADUATE MEDICAL
SCHOOL

ORGANIC CHEMIST required to work on the synthesis of biologically active peptides and peptide analogues in the Endocrine Unit of the Department of Chemical Pathology. Salary in range (£1,812 to £2,448 per annum) according to qualifications and experience. Applications with details of previous experience to Secretary, R.P.M.S., Du Cane Road, London W12 0HS, quoting reference 4/104/N. (1651)

CHAIRMAN—DEPARTMENT OF
ANATOMY

Columbia University, College of Physicians and Surgeons, an equal opportunity employer, is seeking an individual as Chairman of Anatomy Department. Should be qualified medical scientist and experienced medical educator.

Send curriculum vitae to: Myron Winick, M.D., Chairman, Search Committee, Institute of Human Nutrition, 511 West 166th Street, New York, New York 10032 (1289)

MEDICAL RESEARCH COUNCIL

Laboratory Animals Centre

Applications are invited from science graduates (including agriculture) of not less than 28 years of age, for the post of Technical Officer in the Accreditation Department. The post will involve visiting laboratory animal breeding establishments and advising breeders on problems associated with laboratory animal production and supply.

Postgraduate experience with animals or in biological research would be an advantage but not essential.

Salary within the range £2,184 to £3,057 plus London Weighting and superannuation.

Applications, together with a copy of curriculum vitae and the names of two professional referees should be addressed to the Director, M.R.C. Laboratory Animals Centre, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey SM5 4EF. (1725)

VIROLOGIST

UNIVERSITY OF ILLINOIS, URBANA SCHOOL OF BASIC MEDICAL SCIENCES

Opening available September, 1974, for a Ph.D. or M.D. Virologist who will develop a vigorous research programme, teach basic medical virology to medical students in an innovative instructional programme, and participate in the training of graduate students. Applicants must be demonstrably interested in both excellent teaching and research. Rank and salary commensurate with experience and ability.

Submit curriculum vitae, graduate transcripts and names of three references to: Dr Michael J. Weber, Department of Microbiology, University of Illinois, Urbana, Illinois 61801. The University of Illinois is an Affirmative Action—Equal Opportunity Employer, and encourages applications from members of minority groups and women. (1727)

CHELSEA COLLEGE UNIVERSITY OF LONDON

BIOLOGICAL SCIENCES GROUP

A TECHNICIAN, Grade 4, is required as soon as possible to head a small team of technicians responsible for the preparations and maintenance involved in teaching and research in Comparative Physiology and Biochemistry. Salary scale: £2,028 to £2,338 per annum (including London allowance).

Application forms, available from the Departmental Secretary (N), Department of Zoology, Chelsea College, Hortensia Road, London SW10 0QX, should be returned as soon as possible. (1728)

UNIVERSITY COLLEGE HOSPITAL MEDICAL School. POST-DOCTORAL RESEARCH ASSISTANT required for research on the structure and function of avian viruses with particular reference to the mechanisms of viral cytopathology. The appointment will be for two years, salary in the range of £2,385 to £2,550 according to qualifications and experience.—Applications to the Secretary should include detailed curriculum vitae and the names of two referees and quote reference BACT/R.A. (1644)

APPLICATIONS ARE INVITED FROM graduates with an honours degree in Biochemistry for the post of RESEARCH BIOCHEMIST in the Departments of Chemical Pathology and Surgery. The appointed person would work on problems connected with the measurement of catecholamines. Salary within the range £1,566 to £1,980 plus £126 London Allowance.—Applications in writing to: The Secretary, The Medical College of St. Bartholomew's Hospital, West Smithfield, London EC1A 7BE, quoting reference 609. (1677)

UNIVERSITY OF CAMBRIDGE, Department of Genetics. Applications are invited from biologists with experience in *Drosophila* handling to assist in a research project, "An analysis of the fine structure and control of a gene in *Drosophila*", which is being financed by the Medical Research Council for a period of three years commencing January 1, 1974. Two posts are available: (1) ASSISTANT IN RESEARCH. Salary scale £1,752 rising to £2,388, depending on age, etc. (2) RESEARCH TECHNICIAN. Salary scale £1,599 rising to £1,677, depending on age, etc.—Applications with curricula vitae and names and addresses of two referees, should be forwarded to Dr M. Ashburner, Department of Genetics, Milton Road, Cambridge CB2 1XH (1692)

SYNCRYST, CRYSTAL GROWERS AND Consultants, require a TECHNICIAN for interesting and varied work in assisting a small team on several crystal growing projects. We are looking for a young man or woman aged 18-25 with a scientific background and interests in physics and chemistry who can act on their own initiative. Day release is offered to help further his or her career. Salary is negotiable and prospects and benefits are good in our small expanding company.—For further details write or telephone: The Secretary, Syncryst Ltd., Molesey Avenue, East Molesey, Surrey KT8 0RY. Tel. 01-979 3317/3370. (1665)

A TECHNICIAN is required to assist in research concerning corneal graft methods to work in the Eye Bank Laboratory of Moorfields Eye Hospital. Salary in the range £1,440 to £1,845 per annum together with £126 per annum London Allowance.—Applications together with names and addresses of two referees to the Secretary, Institute of Ophthalmology, Judd Street, London WC1H 9QS, by December 15. (1694)

RESEARCH OFFICER IN PHYSICS

Research Officer required for experimental work in fundamental Physics. Experience in nuclear research techniques an advantage. Ph.D. desirable. Salary within the range £1,929 to £2,553 per annum according to qualifications and experience.

Application forms and further details may be obtained from the Deputy Secretary, (N23/11) Birkbeck College, University of London, Malet Street, London, W.C.1. (1693)

ECOLOGIST

Vertebrate ecologist (HSO) required to join team of three investigating farmland ecology. The person appointed will study the predation of partridge chicks by weasels and stoats, commencing January 1974. Must be able to drive and have experience of field work. Curriculum vitae, with three references, as soon as possible to Dr G. R. Potts, Game Conservancy, North Farm, Washington, Fulborough, Sussex. (1716)

ORDER FORM NATURE

To: CLASSIFIED ADVERTISEMENT DEPT., NATURE,
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ADDRESS

FRESHWATER BIOLOGICAL ASSOCIATION

ASSISTANT SCIENTIFIC OFFICER wanted for chemical work at River Laboratory. Five GCE 'O' levels. Starting salary £675 to £1,612 depending on age. Full details from Secretary, Freshwater Biological Association, East Stoke, Wareham, Dorset BH20 6BB (telephone Bindon Abbey 462 314) before November 30. (1650)

UNIVERSITY OF ADELAIDE

Applications are invited for the following appointment: (18604) (3) TEACHING FELLOW IN ORGANIC CHEMISTRY for 1974 from candidates with PhD degrees; to be responsible for practical course including course innovations and to undertake research with existing research groups, which enjoy modern facilities of high standard. (7.12.73)

Salary scale: \$A7,270-286(3)-285(2)-8,698; a non-superannuated and non-tenured appointment.

Further particulars about this post and the conditions of appointment and other information sought will be supplied on request to the Registrar of the University, or to the Secretary-General, Association of Commonwealth Universities (Appts.), 36 Gordon Square, London, WC1H 0PF.

Applications should be sent in duplicate and giving the information listed in the Statement that will be supplied, to the Registrar, the University of Adelaide, North Terrace, Adelaide, South Australia, 5001. (1705)

POLYTECHNIC OF THE SOUTH BANK

DEPARTMENT OF APPLIED BIOLOGY & FOOD SCIENCE RESEARCH POSTS

RESEARCH FELLOW to develop and advance toxicological and pollution studies in conjunction with the Department's research groups working on Fluorides and Potatoes.

RESEARCH ASSISTANT (Fluorides) to assist with analytical work in research into fluorides in food-stuffs.

J. LYONS RESEARCH STUDENTSHIP to undertake research into the action of preservatives in food.

Enquiries to Clerk to the Council (Room 564), Polytechnic of the South Bank, Borough Road, London SE1 0AA. Tel. 01-928 8989. (1679)

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE (University of London)

KEPPEL STREET, GOWER STREET, LONDON WC1

Clinical Nutrition and Metabolism Unit

TECHNICIAN, graduate or H.N.C. required immediately to join an M.R.C. supported group studying problems of biochemical adaptation in relation to obesity and surgical trauma. The group is situated at the Hospital for Tropical Diseases, St. Pancras, NW1. Applicants should have a good biochemical background and laboratory experience. Salary, according to qualifications and experience, within the scale £1,440 to £1,845 plus £126 London Weighting.

Applications, consisting of full curriculum vitae and naming two referees, should be sent to the Secretary (A1) at the School. (1672)

ST. THOMAS' HOSPITAL LONDON S.E.1

RESEARCH ASSISTANT required to work in the Cardiac Surgical Unit at St. Thomas' Hospital on histochemistry of heart muscle and effects of open heart surgery. Salary in accordance with the Whitley Council Junior/Technician scales.

Write or telephone for further details from the Personnel Officer, 79 York Road, London SE1 7NY -01-928 9292 Ext. 2422. (1682)

FELLOWSHIPS AND STUDENTSHIPS

THE UNIVERSITY OF MANCHESTER SIR HENRY ROYCE FELLOWSHIP FOR RESEARCH IN RHEUMATISM

Applications invited for this Fellowship for research into the causes and possible cure of rheumatism and allied diseases. Postdoctoral applicants interested in the biochemistry of collagen or in organ culture of synovia preferred. The Fellow would work as part of a team studying abnormalities of synovial membranes in rheumatoid arthritis and other arthritides. The Fellowship, which is tenable for three years, is valued within the range £1,929 to £2,718 per annum. F.S.S.U.

Further particulars and application forms (returnable by December 8) from the Registrar, The University, Manchester M13 9PL. Quote ref.: 208/73/Na. (1674)

ST JOHN'S COLLEGE, CAMBRIDGE

RESEARCH STUDENTSHIPS

The College invites applications for a number of Research Studentships which are offered to men who are not already members of the College but who propose to register as research students at the University of Cambridge and become candidates for the Ph.D. Degree in any subject. Tenure of each Studentship will be for three years provided academic progress is satisfactory. Candidates will be expected to have gained or to have a strong prospect of gaining a first-class honours degree or its equivalent and election will be contingent upon satisfactory results in such a final degree examination.

The value of the Studentship will normally be such amount as will bring the Student's total emoluments to £795 a year, in addition to the following payments which will ordinarily be made by the College:

- (a) approved University and College fees;
- (b) allowances for dependants;
- (c) a contribution towards expenses of travel from the Student's home;
- (d) allowance for periods of approved postgraduate experience.

Financial assistance may also be given towards the costs of field work, attendance, at conferences and other essential expenses.

Students will be expected to apply for State Studentships or other research awards for which they are eligible.

An unmarried Student can be accommodated in College during his first year of residence and a married Student will usually be offered accommodation close to the College.

Enquiries should be addressed to the Senior Tutor, St. John's College, Cambridge CB2 1TF, to whom completed application forms must be sent so as to reach him by April 1, 1974. (1726)

UNIVERSITY OF LONDON

BRITISH POSTGRADUATE MEDICAL FEDERATION

INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY

330/336 GRAY'S INN ROAD, LONDON WC1

BERNARD SUNLEY RESEARCH FELLOWSHIP

Research Fellow in electron microscopy required for investigation of inner ear, grant-aided for a term of 3 years, which could be suitable for a thesis. Should be graduate in Biology with some E.M. experience. Salary £2,241 rising to £2,559.

Applications with full curriculum and naming referees to the Secretary-Administrator, Institute of Laryngology and Otology, 330/336 Gray's Inn Road, London, W.C.1. (1684)

THE UNIVERSITY OF MANCHESTER

DEPARTMENT OF CHEMISTRY

Applications invited for an S.R.C. POST-DOCTORAL FELLOWSHIP for work on organic photochemical mechanisms. The appointment, initially for one year, will commence on January 1, 1974; salary range per annum: £1,929 to £2,223.

Applications with names of two referees to Dr A. A. Gorman, Department of Chemistry, The University, Manchester M13 9PL. (1660)

UNIVERSITY OF SYDNEY RESEARCH FELLOWSHIP—MEAT SCIENCE

Applications are invited for a Postdoctoral Fellowship in Meat Science at the M. C. Franklin Laboratory of the University of Sydney situated at the University of Sydney Farms, Camden, NSW.

The appointee's first priority will be to prosecute a research programme in Meat Science in a field of his choice, but preferably covering one or more of the following fields: Conversion of muscle to meat; Chemical and biochemical constituents of muscle; The storage and preservation of meat; Factors involved in the eating quality of meat.

The initial appointment will be for one year with some prospect of renewal annually. The successful appointee must hold a PhD in which he has majored in some aspect of Meat Science.

Depending on qualifications and experience, the salary range is \$A7,270-\$A8,413 p.a.

Applications by November 30, 1973, to the Registrar, University of Sydney, NSW 2006, Australia. Enquiries to Dr H. Lloyd Davis, M. C. Franklin Laboratory, University of Sydney Farms, Camden, NSW 2570, Australia. (1706)

THE ROYAL SOCIETY

JOHN MURRAY TRAVELLING STUDENTSHIP IN OCEANOGRAPHY AND LIMNOLOGY 1973

Applications are invited for the above Studentship, open to male or female graduates under the age of 35, for the encouragement of travel and work in oceanography or limnology. This award, which may be held for periods from three months to one year, will in 1974 be up to £1,000, adjusted according to qualifications and place and duration of research. Applications are especially invited from workers in oceanography and limnology, as well as in zoology, botany, geology, mathematics and physics, and it will be permitted to hold the award while receiving a salary from a regular appointment.

Applications receivable by December 15, 1973, should be made on forms obtainable from the Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG. (1643)

THE DENTAL SCHOOL, UNIVERSITY OF BIRMINGHAM

Applications are invited from graduates in Biochemistry or Chemistry for a RESEARCH STUDENTSHIP available in the Department of Oral Pathology in the Dental School. The project, which will be suitable for registration for a Ph.D., is on the subject of the composition and properties of the organic components of biological calcifications. The investigation will have particular reference to dental plaque and its mineralisation but a comparative approach involving study of microbial calcification and both normal and pathological calcifications is envisaged. No specialised dental background is required.—Further details may be obtained from the Assistant Bursar, The Dental School, St. Chad's Queensway, Birmingham B4 6NN, to whom applications, including curriculum vitae and the names of three referees, should be sent by December 10, 1973. (1691)

NEWHAM COLLEGE, CAMBRIDGE

proposes to elect to one or more Research Fellowships, tenable for 3 years from October 1, 1974. Applications are invited from women graduates of any University for research in Biological Sciences or in Philosophy or Psychology, and from women graduates of any University in Great Britain or the Commonwealth for research in any subject.

Unless she receives other emoluments, a Research Fellow who has not yet obtained a PhD will receive £790 a year and free board and residence; or, if she chooses to be non-resident, she will receive £1,012 a year. For a Research Fellow who has already obtained a PhD degree, the emoluments are increased by £147 a year.

The Research Fellow may choose to be pensionable under the FSSU. The closing date for the receipt of completed applications is January 12, 1974.

Full particulars may be obtained from the Principal. (1718)

ROYAL ASTRONOMICAL SOCIETY LEVERHULME VISITING FELLOWSHIPS IN ASTRONOMY 1974-1975

The Council of the Royal Astronomical Society is prepared to receive applications for Leverhulme Visiting Fellowships in the Academic year 1974-1975 (or the calendar year 1975). These awards are open to scholars from the Commonwealth and foreign countries, with a preference for the latter and for those who have not previously had the opportunity of an extended stay in the U.K., who wish to undertake a year's study in any branch of astronomy at a university or another approved institution in the United Kingdom.

Two such Fellowships will be made available. The stipend attaching to each will be in the range £2,200 to £2,600. A contribution towards the cost of the successful applicants' travelling expenses will be made.

Application forms, which must be completed and returned by January 31, 1974, may be obtained from: The General Secretary, Royal Astronomical Society, Burlington House, London W1V 0NL. It is hoped to inform successful candidates by early April 1974. (1675)

AUSTRALIAN NATIONAL UNIVERSITY

Applications are invited for the following:

RESEARCH SCHOOL OF PHYSICAL SCIENCES

POSTDOCTORAL FELLOWSHIPS (43-A22): Appointment will be in the following Departments and Units of the Research School of Physical Sciences:

Department of Engineering Physics: The Department is conducting research in high field magnets, high power lasers, macroparticle acceleration, plasma physics, solar energy conversion, information science and artificial intelligence.

Department of Mathematics: No particular field of research is specified.

Department of Applied Mathematics: The Department has research interests in theoretical colloid science and mathematical vision research.

Diffusion Research Unit: The Unit undertakes studies of the liquid state using isotopic and NMR diffusion measurements.

Electron and Ion Diffusion Unit: The Unit is working in atomic physics with particular reference to low energy electron and ion scattering.

Closing date: January 7, 1974.

FACULTY OF SCIENCE

ARGC RESEARCH FELLOW IN ORGANIC/BIOLOGICAL CHEMISTRY (60-A87): The appointee will be required to work on the chemistry and mode of action of naturally occurring inhibitors of root-strike in Eucalyptus (Tetrahedron Letters, 1971, 1353). The work will be under the direction of Associate Professor W. D. Crow (Department of Chemistry) and Dr D. M. Paton (Department of Botany), and the position is available for one to three years from January 1, 1974. Prospective candidates should hold a minimum qualification of PhD (Organic Chemistry) preferably with some biological background or a strong interest in biological control mechanisms. Synthetic and isotopic tracer work will be involved.

Closing date: December 8, 1973.

Salaries: Salary on appointment will be in accordance with qualifications and experience within the ranges: Postdoctoral Fellow, \$A8,698-\$11,901; ARGC Research Fellow \$A8,698-\$11,901 (2x641; 1x641) p.a. with initial appointment at a level not greater than \$9,980 p.a. (current exchange rates are approximately \$A1:61p:\$US1.48).

Other Conditions: Tenure: Postdoctoral Fellow for not less than one year and not more than two years (two years for overseas appointees). Postdoctoral Fellows would normally have recently completed the PhD degree.

Reasonable travel expenses are paid and assistance with housing is provided for an appointee from outside Canberra. Superannuation (where applicable) is on the FSSU pattern with supplementary benefits.

The University reserves the right not to make an appointment or to make an appointment by invitation at any time.

Further information should be obtained from the Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF. (1719)

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LECTURES AND COURSES

RESEARCH WORKSHOP IN MOLECULAR AND DEVELOPMENTAL BIOLOGY Glasgow—Easter, 1974

A short, intensive, research workshop will be held in Glasgow from 17-30 March 1974. Intended for post-doctoral workers wishing to enter research in the area of common interest to molecular and developmental biologists, in exceptional circumstances post-graduates who could make a significant contribution can be considered. Participants will be asked to contribute to the programme.

A fee of £60.00 will be charged and will cover board and lodging. The workshop is sponsored by SRC and appropriate British participants may have the fee paid in full.

The workshop will be run by the Beatson Institute and the Departments of Botany, Cell Biology, Genetics, Immunology, Microbiology, Virology and Zoology of the University of Glasgow.

Further details, and application forms which should be returned by January 1, 1974, can be obtained from the Secretary, Department of Zoology, Glasgow University, Glasgow G12 8QQ. (1715)

UNIVERSITY OF SHEFFIELD POSTGRADUATE COURSE IN SOLID STATE PHYSICS

The course is designed for postgraduate students who wish to obtain a more advanced background knowledge and further practical training in solid state physics; it will last for one academic year, October to July, ending in an examination for the degree of M.Sc.

Electron states in crystals
Lattice dynamics and related properties
Determination of the structure of solids
Preparation of materials
Physical properties of solids
Magnetism in solids
Physics of semiconductor materials
Solid state devices.

This course has been accepted under the S.R.C. Advanced Course Studentship Scheme.

Further details may be obtained from the Administrative Secretary, Department of Physics, The University, Sheffield S3 7RH. Please quote R95/G. (1700)

UNIVERSITY OF SURREY POSTGRADUATE MEDICAL SUBCOMMITTEE OF SENATE

M.Sc. IN-MEDICAL SCIENCES

The next entry to the M.Sc. in Medical Sciences will be in January, 1974. The course lasts for 2 years all day Wednesdays during the academic terms. The syllabus covers the material for the basic sciences of the primary courses in medicine, surgery, obstetrics and gynaecology, and anaesthetics, but does not exempt students from the relevant primary examinations of the Royal Colleges.

Further details or enquiries may be addressed to the Course Organiser, Dr H. Hillman, Department of Biological Sciences, University of Surrey, Guildford, Surrey. Telephone, Guildford 71281, extension 573. (1532)

UNIVERSITY OF LONDON: A Lecture entitled "Tectonic Evolution of the Southeast Indian Ocean" will be delivered by Dr Dennis Hayes (Columbia) at 5.30 p.m. on November 29 at University College (Gustave Tuck Theatre), Gower Street, W.C.1. Admission free, without ticket. Academic Registrar. (1667)

GRANTS & SCHOLARSHIPS

THE ROYAL SOCIETY

BROWNE RESEARCH FUND

Applications are invited from qualified research workers for personal grants to enable them to undertake research in marine biology at a marine biological laboratory or elsewhere for periods up to twelve months, on the understanding that their university or other post they may hold would meanwhile be kept open for them. Preference will be given to those proposing to work on purely scientific problems. The total amount available for allocation in 1974 will be about £3,000.

Applications receivable by December 15, 1973, should be made on forms obtainable with further details from the Executive Secretary, The Royal Society, 6 Carlton House Terrace, London SW1Y 5AG. (1642)

UNIVERSITY OF MANCHESTER INSTITUTE OF SCIENCE AND TECHNOLOGY

RESEARCH IN CHEMISTRY

Applications are invited from British graduates, Grad.R.I.C., etc., for grants for Ph.D. research available from January 1, 1974.

- (1) Synthetic Organic Chemistry
- (2) Organic Reaction Mechanisms
- (3) Medicinal Chemistry
- (4) Homogeneous Catalysis of Petrochemical Products
- (5) Olefin Chemistry.

Applicants should write as soon as possible to Professor R. N. Hazeldine, Department of Chemistry, U.M.I.S.T., Manchester M60 1QD. (1699)

AUSTRALIAN NATIONAL UNIVERSITY RESEARCH SCHOOL OF BIOLOGICAL SCIENCES

RESEARCH SCHOLARSHIPS

Two PhD scholarships are available in the Research School of Biological Sciences in the following areas:

PROTEIN CHEMISTRY/TAXONOMY

The project is concerned with investigating taxonomically patterned variation, of nutritional interest in amino-acid composition of leaves and seeds. The work will involve isolation and characterisation, with amino-acid analyses, of proteins from a range of plant materials.

Enquiries should be addressed as soon as possible to Dr E. H. Creaser or Mr L. Watson, Research School of Biological Sciences, P.O. Box 475, Canberra City ACT 2601, from whom further information may be obtained.

ENVIRONMENTAL BIOLOGY

The scholar would work under the direction of Dr I. R. Cowan on either: (a) physics of gas and vapour exchange and its control in leaves of higher plants; (b) ecological aspects of stomatal physiology.

Applicants should have, or expect to have, a B.Sc. (Hons) or M.Sc. in an appropriate area of biology and a keen interest in the application of physics and mathematics to biological problems.

Application forms are available from the Academic Registrar, P.O. Box 4, Canberra, ACT 2600, Australia.

Scholarship Conditions: ANU research scholarships are awarded for three years and provide a yearly tax free allowance of \$A3,290, with extra allowances for dependent spouse and children. Return fares to Canberra and a grant for removal expenses are normally paid. Assistance with accommodation is available. (1707)

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Editors
G A KERKUT and J W PHILLIS

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J Bjaeldel Departments of Neurosurgery and Physiology, University of
Minnesota Medical School

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G I Drummond Department of Pharmacology, School of Medicine,
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The present ICI scheme for the award of postdoctoral research Fellowships covered the period 1968/9-1972/3. With its termination, the Company has undertaken to support a new scheme, more closely allied with its own activities, for a further three-year period 1973/4-1975/6.

Applications are invited for awards under the new scheme for the academic year 1974/5. Fellowships may be held at the universities listed below. Additionally, up to five of the Fellowships may be held at appropriate European research centres.

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University of Aston in Birmingham
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The Queen's University of Belfast
University of Birmingham
University of Bradford
University of Bristol
Brunel University
University of Cambridge
The City University
Cranfield Institute of Technology
University of Dublin, Trinity College
University of Dundee
University of Durham
University of East Anglia
University of Edinburgh
University of Essex
University of Exeter
University of Glasgow

Heriot-Watt University
University of Hull
The National University of Ireland
(*Dublin, Cork, Galway*)
University of Keele
University of Kent at Canterbury
University of Lancaster
University of Leeds
University of Leicester
University of Liverpool
University of London
Loughborough University of Technology
University of Manchester (*including University of Manchester Institute of Science and Technology*)
University of Newcastle upon Tyne
University of Nottingham

The Open University
University of Oxford
University of Reading
University of St. Andrews
University of Salford
University of Sheffield
University of Southampton
University of Stirling
University of Strathclyde
University of Surrey
University of Sussex
University of Ulster
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University of Warwick
University of York

The Fellowships, tenable for two years, can be held in any field relevant to ICI's own research interests: this includes many branches of chemistry, physics, the biological sciences, applied mathematics, engineering, and technology. For the guidance of the universities and intending candidates an exemplary list of research topics is available. Candidates should not be more than 28 years of age on taking up their awards, and must hold the Ph.D. degree or have equivalent research experience. Successful candidates will be expected to commence their Fellowships on 1st October, 1974.

The stipend will depend upon age and experience but will generally be within the range £2,000-£2,500 per annum, together with FSSU benefits. In the case of Fellows working at a European research centre an appropriate adjustment will, if necessary, be made to cover differences in the cost of living, and a contribution will be made towards travelling expenses.

Forms of application may be obtained from the Registrar/Secretary of the university at which

the candidate wishes to pursue his research (except in the case of London University, where enquiries should be directed to the Academic Registrar), and must be returned duly completed by 8th January, 1974. Candidates desiring to work in Europe (and only those candidates) should apply to Dr. T. I. Williams, Research and Development Department (Academic Liaison), Imperial Chemical House, Millbank, London SW1P 3JF. Candidates need apply to only one university, but may apply to not more than three if they so wish. In the case of multiple applications, separate forms must be completed in respect of each university. Among other information, candidates will be required to submit a brief *curriculum vitae*, a clear summary of the research programme proposed, and the names of two referees. Other things being equal, preference will be given to candidates proposing to carry out their research at institutions other than that from which they make application.

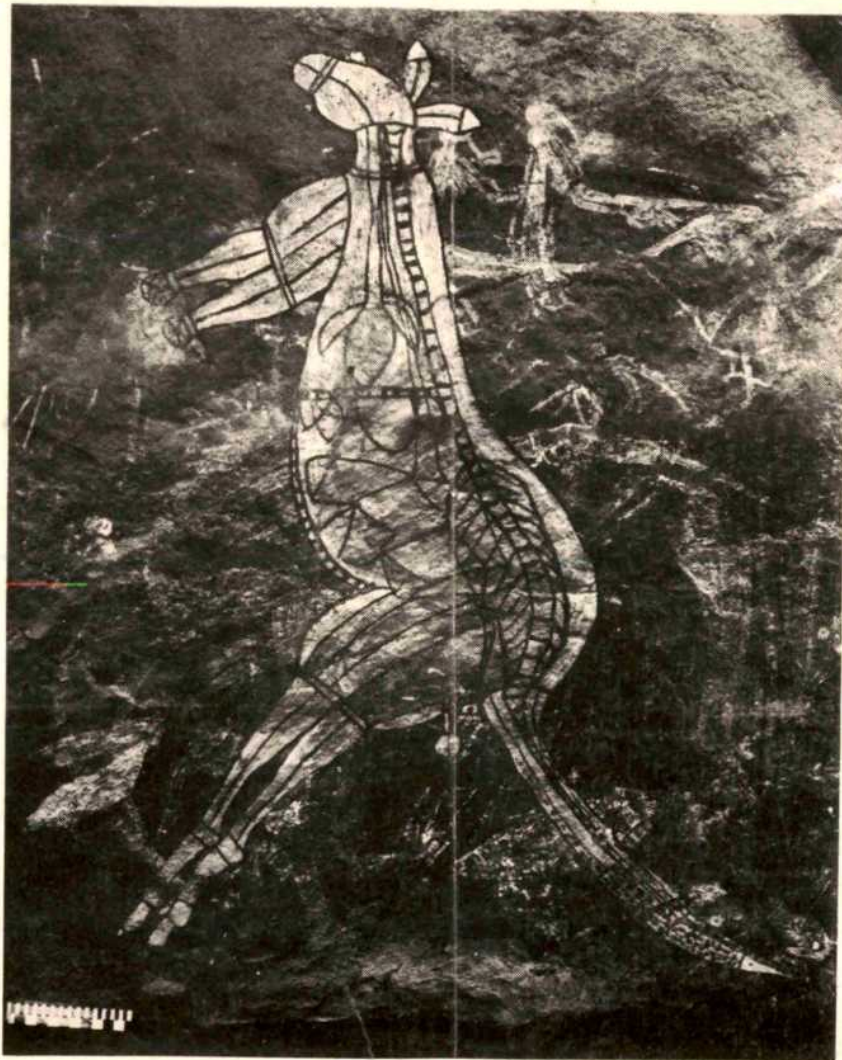
The final choice of candidates will be made by a National Selection Committee, comprising representatives of the universities and of ICI.

NATURE

Vol 246 No 5430

November 30 1973

FRIDAY



Rock art



Science in Australasia

Cell

Cell publishes papers of general interest in cell and viral biology, including molecular biology, cell biology, tumor virology and immunology, genetic development and related areas. **Cell** also includes reviews, discussions of new books and accounts of meetings. Research papers will be refereed within a short time of submission and accepted articles will be published within three months. Manuscripts and editorial correspondence should be addressed to the Editor or European Editor.

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Cell is published at monthly intervals by The MIT Press. The contents of the first issue, of January 1, 1974 are:

Genetically directed preferential X-activation seen in mice: U. Drews, S. R. Blecher, D. A. Owen and S. Ohno

Ouabain-resistant mutants of mouse and hamster cells in culture: R. M. Baker, D. M. Brunette, R. Mankovitz, L. H. Thompson, G. F. Whitmore, L. Siminovitch, and J. E. Till

A uridine kinase-deficient mutant of 3T3 and a selective method for cells containing the enzyme: L. Medrano and H. Green

SpoT, a new genetic locus involved in the stringent response in *E. coli*: T. Laffler and J. Gallant

The messenger-like poly-A containing RNA species from the mitochondria of mammals and insects: M. Hirsch, A. Spradling and S. Penman

Existence of methylated messenger RNA in mouse L cells: R. P. Perry and D. E. Kelley

Arrangement of specific oligonucleotides within poly-A terminated Hn RNA molecules: G. R. Molloy, W. R. Jelinek, M. Salditt and J. E. Darnell

Mixed splenocyte cultures and graft versus host reactions selectively induce an "S-tropic" murine type C virus: C. J. Sherr, M. M. Lieber and G. J. Todaro

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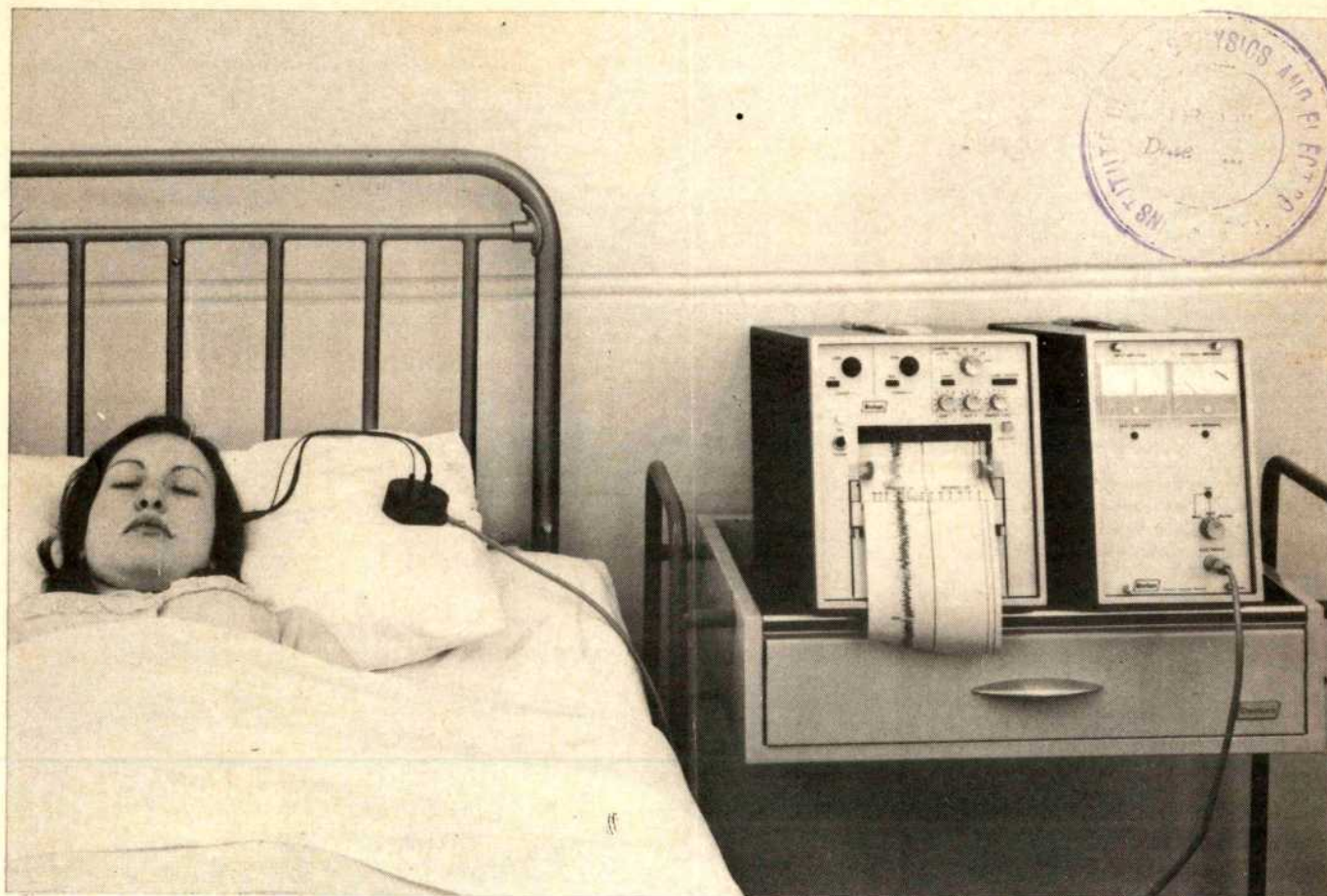
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edited by MORRIS ROCKSTEIN, University of Miami

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	Page		Page
What is in a <i>Nature</i> Paper?	237	Emerging Picture of Pleistocene Australians—JONES (ANU)	278
Guide to Authors	238	Prospects for Astronomy in Australasia—BOLTON (CSIRO, Sydney) and CANNON (UK 48-inch Schmidt Telescope Unit, Edinburgh)	282
NEWS		Hundred Years Ago	287
New Rules for Biomedical Research Projects		ARTICLES	
Education/More on Medical Ethics/Soviet Science/ Nuclear Weapons/Short Notes	239	Hot spots—Relative motion of hot spots in the mantle —MOLNAR and ATWATER (California, San Diego)	288
NEWS AND VIEWS		Plasma membrane—Plasma membrane assembly during the cell cycle—GRAHAM (Imperial Cancer Research Fund, London), SUMNER, CURTIS and PASTERNAK (Oxford)	291
Role of Sex-linked Histocompatibility Antigens/Hot Spots Must Move / Systematic Zoology / Cyclic AMP / Medical Genetics / Hormones / Pest Control / Neurochemistry / Moose / Microearthquakes / Quasars / Nuclear Structure	243	LETTERS TO NATURE	
SCIENCE IN AUSTRALASIA		Physical Sciences	
Funding and Control of Australian Science—ROBERTSON (ANU)	252	QSOs—Interpretation of Hubble diagram — STANNARD (Jodrell Bank)	295
New Zealand's National Research Advisory Council—BROWN (NRAC, Wellington)	255	Mid-Atlantic Ridge—A median valley refraction line—WHITMARSH (IOS, Godalming)	297
Scientific Research in New Zealand—POLETTI (Auckland)	257	Thermonuclear fusion—Attainment of gigavolt potentials by magnetic insulation—WINTERBERG (Nevada System)	299
Science under an Australian Labor Government—POCKLEY (New South Wales)	260	Solar activity—Acceleration and injection of electrons during August 1972 event—MACCAGNI, PEROTTI, VILLA (CNR, Milan), CHERKI, RAVIART and TREGUER (CENS, Saclay)	300
Seismological and Geothermal Research in New Zealand—ADAMS and HATHERTON (DSIR, Wellington)	262		
Earth Sciences and the Australian Continent—McELHINNY (ANU)	264		
Pest Management in Australia—WATERHOUSE (CSIRO, Canberra)	269		
Solar Power in the Australian Energy Scene—MORSE (CSIRO, Hightett)	271		
Rock Art in Australia—EDWARDS and UCKO (Australian Institute of Aboriginal Studies Canberra)	274		

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 245 to 249.

(Continued overleaf)

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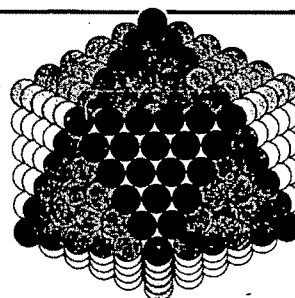
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	Page
Exobiology —Monocarboxylic acids in Murray and Murchison meteorites—YUEN and KVENVOLDEN (NASA-Ames, Moffett Field)	301
Australian prehistory —Pleistocene human occupation site in Buchan, south-east Australia—FLOOD (ANU)	303
Biological Sciences	
Collagen mRNA —Translation of messenger from chick embryo calvaria in a cell-free system derived from Krebs II ascites cells—BENVENISTE, WILCZEK and STERN (NIH, Bethesda)	303
Macrophages —Production by stimulated macrophages of factors depressing lymphocyte transformation—NELSON (Sydney)	306
Sex ratio —Decrease in progeny of mice inseminated with sperm treated with H-Y antiserum—BENNETT (Cornell) and BOYSE (Sloan-Kettering Cancer Center, New York)	308
Plant pathology —Induction of cell wall degrading enzymes in vascular wilt fungi—COOPER and WOOD (Imperial College, London)	309
Soil fungistasis —Caused by ethylene—SMITH (Biological and Chemical Research Institute, NSW, NSW)	311
Kangaroo locomotion —High speeds at low cost—DAWSON and TAYLOR (Harvard)	313

BOOK REVIEWS

	Page
The Female Orgasm: Psychology, Physiology, Fantasy, Seymour Fisher (A. J. COOPER)	315
Regulation in Metabolism, E. A. Newsholme and C. Start (A. R. HIPKISS)	315
Genetic Control of Immune Responsiveness: Relationship to Disease Susceptibility, Hugh O. McDevitt and Maurice Landy (editors) (E. GÜNTHER)	316
Electrochemical Systems, John S. Newman (H. R. THIRSK)	316
The Cell Cycle in Development and Differentiation, M. Balls and F. S. Billett (editors) (J. B. GURDON)	317
Ultrastructure of Rat Adenohypophysis: Correlation with Function, Allen Costoff (C. L. FOSTER)	317
Radiation Chemistry, A. J. Swallow (G. V. BUXTON)	317
Problems in Materials Science, vol. 1, H. D. Merchant (editor) (R. W. CAHN)	318
Pacific Fishes of Canada, J. L. Hart (ALWYNE WHEELER)	318

TELEVISION REVIEW

Black Holes — Authorised Version (EDWARD PHILLIPS)	319
--	-----

CORRESPONDENCE

Open Journal (F. Peter Woodford), Arginine Deficiency (A. ARNOLD)	319
Announcements—University News/Miscellaneous/International Meetings	320

Next Monday's issue will include

- Sun**—Faculae and the '25-day' solar fluctuation—CHAPMAN (Aerospace Corporation, Los Angeles) and INGERSOLL (CalTech)
- Astronomy**—Infrared heterodyne detection of the Moon, planets and stars at 10 μm —De GRAAUW and Van De STADT (Utrecht)
- Lunar fines**—Relaxation times of remanent magnetisation—TSAY (CalTech)
- Carbon fibres**—Anomalous behaviour on prolonged oxidation—HART and PRITCHARD (Kingston Polytechnic, Surrey)

Next Wednesday's issue will include

- Transfer RNA**—Specific recognition of GT Ψ C loop by 50S ribosomal subunits from *E. coli*—RICHTER, ERDMANN (Max-Planck, Berlin) and SPRINZL (Max-Planck, Göttingen)
- DNase**—DNA sequence restricted by restriction endonuclease AP from *Haemophilus aphrophilus*—SUGISAKI and TAKANAMI (Kyoto)
- HCG**—Leydig cells of immature rats insensitive to gonadotrophin contain HCG receptor—FROWEIN, ENGEL (Freiburg) and WEISE (Hamburg-Eppendorf)
- Genetics**—Partial fertility of artificial hybrids between Asiatic and American cockleburs—McMILLAN (Texas)

Elementary Principles of Probability and Information

R. F. Wrighton

December 1973, viii+92 pp., limp cover, £1.95/\$5.50

0.12.765550.6

This book provides an overdue synthesis at an elementary level between two disciplines. Dr Wrighton deals with some of the dilemmas which confront students of recent advances in problems at the interface between relatively new theories of information and traditional probability theory. The link he forges between the two enables the author to provide a fresh approach to problems which have been the subject of prolonged controversy, and some of the conclusions he reaches suggest a radical re-appraisal of the role of statistical experimentation in the medical, biological and associated sciences.

The Chemistry of Electrode Processes

Ilana Fried

November 1973, x+226 pp., £4.90/\$13.75

0.12.267650.5

To achieve her aim of providing a concise introduction to the study of electrode processes (electrodics), the author has separated this work into three basic divisions—fundamentals, experimentation, and applications. It is her belief that the study of this text will enable the reader to proceed with the use of electrodes in an intelligent, informed manner within his own specific area of interest.

Contents: Introduction. The Galvanic cell, basic definition and concepts. Electrode kinetics. The electrode-solution interphase at equilibrium. Techniques of measurement. Some technological aspects of electrodes. Bibliography. Subject index.

Linnaeus's Öland and Gotland Journey 1741

Translated from the Swedish edition 1745, by Marie Åsberg and William T. Stearn

December 1973, iv+228 pp., 12 plates, £6.00/\$17.00

0.12.064750.8

In 1741 Carl Linnaeus was sent to the Baltic islands of Öland and Gotland to survey their natural history, economic products and potentialities. Four years later he published a journal describing this journey, a fascinating medley of information written in a simple, direct but lively style. Linnaeus recorded the presence of many life-forms existing at the most northerly outpost of their geographical range—this examination of the two islands as their restricted type-locality holds considerable scientific importance. The journal also contains details of rune stones and information of historical, archaeological and folk-lore interest, and should appeal to the traveller as well as the taxonomist and natural historian.

High Voltage Electron Microscopy

Proceedings of the Third International Conference

Edited by P. R. Swann, C. J. Humphreys and M. J. Goringe

December 1973, xii+476 pp., £7.00/\$19.75

0.12.678750.6

The book forms the full proceedings of the Third International Conference on High Voltage Electron Microscopy held in August 1973 at St Catherine's College, Oxford, under the auspices of the Royal Microscopical Society. It aims to present a comprehensive treatise on the latest developments and applications of high voltage electron microscopy. The editors intend that the book will provide a valuable source of reference for workers in the field and introduce to others the capabilities and potential applications of high voltage electron microscopes.

Interrelationships of Fishes

Supplement No. 1 to Volume 53 of the Zoological Journal of the Linnean Society

Edited by P. H. Greenwood, R. S. Miles and Colin Patterson

December 1973, xvi+536 pp., £11.00/\$31.00

0.12.300850.6

This volume provides an almost complete coverage of current thinking on anatomical, phyletic and other research relating to hypotheses on the phylogeny of fishes. It is the only book of its kind available to students, teachers and research workers in the field of lower vertebrates. A highly original reference work, it will be of great use to those working or teaching in evolutionary biology, vertebrate anatomy, ichthyology, palaeontology and taxonomy as well as to those using fishes as experimental animals.

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What is in a *Nature* Paper?

TODAY a new guide to authors is published. This is hardly a momentous event but it does provide an opportunity to discuss in some detail both the form and the content of material submitted to *Nature*. Any journal that attempts to span the sciences and, in addition, is constrained in the number of papers that it can publish is bound to be subjected to continued questioning both internally and externally.

Is there any future for a journal like *Nature* that tries to skim the cream of many sciences and, what is more, claims that its papers should be readable by those beyond the immediate confines of the speciality? At a time when a typescript can be submitted, refereed, printed and published in three months in some specialist journals, what attraction does a general journal have as a vehicle for publication?

The most obvious answer, and the one most commonly given, is that the existence of *Nature* allows a scientist with an idea which he thinks has implications beyond his own field to tell it to the community at large, and that this is a good thing. No doubt there is something in this, although perhaps less than is sometimes claimed. Much lip service is paid to cross fertilisation and conferences are devoted to bringing together different disciplines but many of these have all the features of sporting encounters. The sides arrive separately, are intent on demonstrating their own skills, are unimpressed or ignorant of the skills of others and retire to separate dressing rooms at the end. The actual transmission of ideas between disciplines is probably most effectively done by a very few bright people prepared to spend months reading, talking and thinking.

Nonetheless papers in *Nature* do get read and understood by more than the specialists and for want of a better term we call this 'reading for pleasure'. There is a large readership genuinely interested in where science has got to and what problems are being attacked this year. The wide range of correspondence received in the *Nature* office indicates clearly that this interest in the results of present research is not confined to scientists. Moreover, in many parts of the world the library budget restricts very severely the number of specialised journals available. Here *Nature* plays an even bigger role. It is not functioning simply as a journal for announcing results and providing reading for pleasure—for some it is the only way to keep abreast.

We thus see no reason why a general journal should not flourish and should not, with some justification, invite scientists to continue to send material to it.

The obvious follow-up question is—what material? *Nature* clearly cannot claim to be all-embracing. In some fields, in spite of corrective action in "News and Views", papers are rare. This is not the result of any conscious policy; indeed we would welcome more frequent contributions in, say, nuclear physics, but the structure of some branches of science is now so mature, even middle-aged, that the specialist journals provide all that practitioners need. It cannot be denied, however, that there is among

scientists a general body of ignorance which leads to antipathy towards developments in fields in which authors rarely reach out to a more general readership.

The qualities that are sought in manuscripts are immediacy, wide interest, clarity and plausibility. We seek first to have some positive reason for publishing, and a reason which is related to the state of science at present. Will we be impeding science by declining to give the paper a rapid, wide circulation?

We next ask whether the paper will have a broad appeal. It is not easy to determine the breadth of appeal but many authors make our job even more difficult by failing to provide an inkling of why the paper is appealing. It is not good enough for a paper to be technically correct; it must do a certain amount of self-advertisement. Most readers are not prepared to pitch into a paper unless they have some idea what it is about. It is surprising how little the journalist's most elementary skill has permeated the scientific profession—the first paragraph tells the story, the rest fills in the details. We venture to suggest that a good uncomplicated first paragraph more than doubles the numbers of those who will read a paper right through and ensures an enormous increase in those who will at least give the paper attention for a brief period.

Finally, plausibility. Does the paper carry a message which a reasonable man could take seriously? Does it hang together? Does it avoid the devious? It is easier to define plausibility through such questions than through assertions. Plausibility does not rule out controversy, but it does eliminate irrationality.

One rather well-worn hurdle remains—brevity. We give some guidelines about the upper limits to length, fully expecting these limits to be breached. Nevertheless it bears repetition that the size of *Nature* is limited, so long papers simply exclude others. Authors are well advised to think carefully whether they are planning an

100 Years Ago



THE Cape mail brings word that the *Challenger* has arrived at Simon's Bay. On her voyage from Bahia she touched at Tristan d'Acunha, and made a survey of the groups of islands to which it belongs. Two Germans were found who had lived there for a couple of years, and who gladly availed themselves of the opportunity of leaving.

From *Nature* 9, 92, December 4, 1873.

article or a letter. Letters tend to have a more immediate urgency and articles a more expanded viewpoint; it would be wrong to regard a letter as a failed article. We deliberately make no distinction in textual type size between the two, in order not to diminish the great importance we attach to letters.

Some of *Nature's* distinctive requirements, sometimes criticised, should be viewed in the light of a desire to publish more papers. Expansive and fulsome acknowledgements are frowned upon—A. V. Hill's splendid send-up (*Nature*, 175, 266; 1955) is well worth reading. References are numbered but the idea is not to irritate by adopting a system different from most others, rather to save up to half a line per reference. Thereby we can publish perhaps three more letters per week. For similar

reasons, the number of references should be kept firmly in check.

With the absorption of *Nature Physical Science* and *Nature New Biology*, it is only reasonable to ask whether there is to be less space for papers which in the past three years have gone to the 'satellites'. The answer, in the short term, is no. The situation in the medium and long term depends as much as anything on trends in science and the world shortage of printing paper. We are, however, adding a section as an experiment. Matters butions following up earlier material. It is more extensively described below.

It is impossible to run a journal that tries to be selective without generating mixed feelings and some controversy. We shall continue to attempt to avoid blandness.

Guide to Authors

MANUSCRIPTS submitted to *Nature* must contain original work and not be under consideration elsewhere simultaneously. The Editor is guided by referees and his decision on acceptability is final. The editorial staff cannot discuss decisions over the telephone.

Nature accepts three types of communications: Articles, Letters, and Matters Arising. Articles are up to 3,000 words in length with at most six figures and may either be reports of major research developments in a subject or broader reviews of progress. *Nature* commissions many of the latter and authors considering preparing a review are urged to consult the Editor first. Letters are brief reports of research of unusual and wide interest. They should not in general be longer than 1,000 words; at most they may have three or four figures. 'Matters Arising' is a new feature intended to permit occasional short discussion of papers that have previously appeared in *Nature*. A limit of 350 words is placed on contributions in this category. Points raised in 'Matters Arising' must have the same general interest and substantive character that is expected of original *Nature* papers. Authors will be invited to reply briefly to such discussion of their work; the Editor will decide on suitability of any exchange for publication, if necessary after consulting a referee.

Manuscripts should be submitted either to London or Washington but manuscripts declined by one office will not be reconsidered by the other. Two typed copies should be submitted, each including lettered copies of figures. Typing (including references) should be double spaced. The title should be brief and informative. Pages should be numbered. References, tables and figure legends should start on separate pages. Authors are reminded that experimental detail vital to the paper yet which would interrupt the narrative is best placed in the figure legends. Units should conform to the *Système International*. Greek characters should be identified in the margin on their first appearance. Equations should occupy single lines if possible. $\exp(a)$ is preferred to e^a if 'a' is more than one character.

Articles should be accompanied by an abstract of not more than fifty words, and the abstract should list the main conclusions that are drawn. Sub-headings

may be supplied for articles, but should carry more information than, say, 'Introduction', 'Experiments', 'Conclusion'.

References are indicated by superscripts in the text. The style of references may be gleaned from any contemporary *Nature* with the following two changes:

- (i) If it is necessary to refer to several references by the same author at once, only one reference number need be given.
- (ii) The last page as well as the first of any reference should be cited.

Abbreviations for references should follow the *World List of Scientific Periodicals*, fourth ed., (Butterworth, 1963-65). 'Personal communication' and 'unpublished work' do not go in to references and should be incorporated in the text. Papers in preparation and submitted for publication likewise should not appear in references—'in the press' is the earliest that a paper may be referred to. Footnotes are not permitted.

Acknowledgments should be brief. Grant numbers, statements that the work is contribution number 999 of the institute, declarations that the director has authorised publication or announcements that the order of authors has been chosen by lot are not printed.

Original artwork should be sent with the manuscript. All artwork should be clearly marked with the author's name and an indication of which way up it is to appear. Line drawings should preferably be in Indian ink on heavy cartridge paper, although other materials are acceptable; however, thin, shiny, folded, torn or heavily handled material should be avoided. Matt rather than glossy photographs are preferred. Figures are usually reduced to one column width, and the originals should be about twice their final size. Figures, particularly maps, should contain nothing but essential material. It is preferred that the original be unlabelled but with an attachment of the same size containing the appropriate lettering. Labelling on photographs should if possible be avoided entirely.

The Editor will be glad to answer questions on any matters relating to this guide.

NEWS

New Rules for Biomedical Research Projects...

by our Washington Correspondent

FUTURE participants in biomedical research projects in the United States may have good cause to be thankful for the publicity accorded to some 200 black men from Tuskegee, Alabama, who took part, without their knowledge or consent, in one of the most highly publicised medical research scandals to come to light in recent years. The furore that broke out when details of the project were unearthed last year has led to a searching re-examination of ethical standards in clinical research and the prospect of a set of new regulations designed to safeguard the rights of experimental subjects in such research.

The Tuskegee study, as it quickly became known, was originally sponsored by the federal government and was designed to determine the clinical effects of syphilis and the efficacy of treatment for the disease. The procedure was simple. A number of poor black men from rural Alabama who were known to have syphilis in the 1920s were denied treatment for some 40 years while the course of the disease was monitored. None of them was ever told that he had syphilis, many died and the rest were quietly forgotten until the whole affair hit the headlines.

The Department of Health, Education and Welfare (HEW) immediately set up an official inquiry into the matter, and the committee had little difficulty in concluding that the study was ethically unjustified. The Tuskegee study had, for a start, violated the cardinal rule in human experimentation—that subjects should be informed of the likely risks and that they should freely consent to take part. Moreover, no risk-benefit analysis of the study could conceivably have shown that the benefits to be derived would ever outweigh the risks to the unfortunate men who unwittingly took part.

The committee also suggested that the present guidelines governing clinical research are vague and that they are probably not strict enough to discourage less scandalous, but still unacceptable, research projects. In the meantime, Senator Edward M. Kennedy was holding a series of hearings with his Senate Health Subcommittee which bore out the committee's fears in brutal detail. Kennedy's hearings turned out to be a nicely stage-managed exposé of a number of research projects whose ethical foundations ranged from outrageous to merely dubious.

The upshot of Kennedy's hearings was a bill to strengthen the review procedures for all research projects involving human subjects, to establish in the federal government a high level board to draw up policies for protecting research subjects, and to ensure that the policies will be implemented at the institutional level. The bill has been passed by the Senate, but it is now in limbo, awaiting a conference committee to put it into final form.

The Administration has also been busy, for apart from setting up the com-

mittee to investigate the Tuskegee study, the Department of HEW has recently proposed a set of guidelines which will eventually require institutions in receipt of HEW grants to tighten up their control of experiments involving human subjects. Finally, an *ad hoc* committee consisting of members of the National Institutes of Health (NIH), the National Institute of Mental Health and the Food and Drug Administration last week published a draft report recommending tight controls on research involving children, prisoners, the mentally

EDUCATION

Open to All?

THE Vice Chancellor of the Open University, Dr Walter Perry, persuaded the producer of *Coronation Street* to enrol Mrs Clegg, who keeps the corner shop, at the Open University. Sadly her progress is rarely mentioned, but she has at least helped to ensure that 40% of the British population have heard of the Open University.

Dr Perry gave the third Shoenberg memorial lecture to the Royal Television Society last week. He described how the Open University has coped with the momentous task of giving a university education, at a distance, to students of whom no formal entrance qualification is asked.

Very little has been spent on advertising, and consequently Dr Perry considers the number of people who have heard of the Open University as quite encouraging. But the 60% who have not heard of it are mainly from the lower socio-economic groups, for whom it was primarily created.

Of the 36,000 or so prospective students who have applied each year, 10% have no academic qualifications and 30% have some qualifications, but less than those required by other British universities. The remainder could have entered a more conventional British university.

The Open University is thus not yet appealing to those it wishes to attract. Many have obviously not heard of it, and Dr Perry feels that some have a typically British suspicion of all things intellectual.

How do the unqualified 10% fare? Courses assume no previous knowledge but progress quickly. During the first three months of tuition slightly more

out. Of the ones who progress further the unqualified students perform indistinguishably from the others in arts subjects, slightly less well in science and technology and very badly in mathematics. The cure for this has not yet been found: should the first year mathematics course be altered? Should the Open University alter its philosophy and impose entrance requirements for mathematicians, or should it provide pre-university mathematics courses itself?

Everyone is agreed that the courses for the first two years should be general in scope but many students now approaching their third and fourth years wish to progress to more specialised courses. Some members of the Open University are ready to provide them; others contend that the educationally deprived students who have yet to enrol in large numbers will not want conventional specialised courses. There is not enough money for both types of course and discussion is heated.

The drop-out rate in many conventional correspondence courses is about 90%. Dr Perry and his colleagues have, however, managed to keep the rate below 30%, partly by modelling several features of the Open University, such as the week-long summer school, on the similarly successful correspondence University of New England in Armidale, New South Wales. Revolutionary teaching methods such as home experiment kits and tape recordings have quickly become incorporated into courses.

The Open University is no longer a topic of party political dispute, and the sale of its courses for use in other universities may make it the most cost-effective university in the world. If it can succeed in appealing to the section of the population it has not yet touched,

infirm and other special cases.

The publicity given to research projects that are plainly outrageous has, however, tended to overshadow some of the more delicately balanced arguments and concerns. For example, what controls should be applied to research on children who lack not only the legal capacity to give their consent to take part but who may also be unable to understand the possible risks? Another area fraught with difficulty is research on prisoners—for example, is a man who is denied basic freedoms and who is continuously subject to the will of prison authorities truly free to give his consent to anything? Moreover, does the opportunity to take part in a research project which will relieve the routine of prison life and which may involve other large rewards carry undue incentives which, to him, outweigh the risks? (More than 70% of preliminary human testing of drugs in the United States is carried out on prisoners.) Equally difficult questions are raised in connection with research on the mentally retarded, on fetuses and on pregnant women.

It was those tricky questions that were faced by the *ad hoc* NIH committee, whose recommendations were published last week in the *Federal Register*. The committee believes that controls on such research should be greatly strengthened at both the federal level and in the institution in which the experiments will be conducted and it also suggests a few cases in which human experimentation should be outlawed entirely.

As far as research on children is concerned, the committee suggests that any proposal should be reviewed for ethical considerations by at least three committees, two of which would be in the institution in which the research is to be carried out and one in the agency sponsoring the research. It would work like this. Before submitting a proposal to HEW for funding, the project must be reviewed by an Organizational Review Committee, consisting of members drawn from a variety of disciplines, some of whom would not be employed by the institution concerned. Once the committee has approved the experimental procedures, the proposal would then be sent to HEW, where it would be subjected to the usual peer review system for scientific merit. The next stage is review by special committees to be established in every agency of HEW. These Ethical Review Boards would again consist of members from various disciplines and, as well as examining individual projects, they would advise the agency on general ethical issues.

Once approved by this process, the project would then come under the supervision of yet another institutional review committee, the Protection Com-

mittee. Its duties would be to ensure that those who take part in the experiment are fully informed of the risks, and that their consent and that of their parents is freely given. The Protection Committee would also be on hand to make sure that participants could pull out at any stage if they so wished.

In addition to that mechanism, the committee also suggests a number of other criteria that should be met before research can be carried out on children. First, the consent of both parents should be obtained. Second, the consent of any child over the age of seven who takes part in an experiment should be obtained. Finally, children without natural or adoptive parents, or those detained in an institution or in court, should be excluded from participating.



Senator Edward Kennedy

As for research on prisoners, the committee notes that it is ultimately up to the courts to decide whether prisoners are in a position to give consent without undue coercion, but it points out that in the meantime HEW should adopt a set of regulations which afford prisoners as much protection as possible. In short, the committee suggests that a project involving prisoners should come under the purview of a Protection Committee consisting of at least five members, one of whom would be a prisoner. It would make sure that those who take part are given full information and that they are not offered undue incentives.

Finally, the committee suggests that research should be carried out on the mentally infirm only if it can be proved that the study cannot be accomplished with the use of other volunteers; that no research should be performed on the abortus if it involves prolonging the heartbeat and respiration or, conversely, if it will of itself terminate the heartbeat; and that no research involving implantation of human ova which have been fertilised *in vitro* shall take place until animal studies have indicated that it would be safe (and that includes studies of the naturally born offspring

MORE ON MEDICAL ETHICS

... But Britain Differs

CLINICAL research investigations of children and mentally handicapped people should be allowed, according to a committee of the Royal College of Physicians. In a report published today on the *Supervision of the Ethics of Clinical Research Investigation in Institutions* (£0.10 from the Royal College) the committee says that to ensure advances in medical treatment research must continue, even though the investigations might not be of direct benefit to the patient.

The committee adds, however, that the investigation should be carried out "only when the procedures entail negligible risk or discomfort and subject to the provisions of any common, or statute, law prevailing at the time".

The Royal College document is in sharp contrast to the report of the *ad hoc* committee of members of the National Institutes of Health, the National Institute of Mental Health and the Food and Drug Administration published last week in the United States (see page 239). The report from the United States, which is likely to be incorporated into firm proposals by the Department of Health Education and Welfare, recommends much more stringent controls on clinical research than does that from the Royal College.

The Royal College report is a sequel to one published by the same body in 1967. Sir George Godber, Chief Medical Officer at the Department of Health and Social Security (DHSS), wrote to the late Lord Rosenheim, then president of the college, in 1971 asking him to investigate further the supervision of the ethics of clinical research in institutions. In particular, Sir George asked advice about the composition of ethical committees and the scope of clinical investigations.

The advice now given to the DHSS is that ethical committees should be small and should be constituted so that they do not "cause an unreasonable hindrance to the advancement of medical knowledge". The members should be experienced clinicians but there should also be one lay member. The committee stresses that this lay member must be someone "who is not associated with the [medical] profession in any paramedical activity". Biochemists and psychologists are therefore ruled out.

In view of the uncertainty about the procedures which have to be referred for approval, the Royal College advises that application should be made to an ethical committee "for all proposed clinical research investigations". The committee stresses the fact that a drug which has been granted a Clinical Trial Certificate or a Product Licence by a

ation of the Committee on Safety of Medicines "in no way absolves the ethical committee from investigating the ethical aspects of that trial".

Patients who are undergoing tests which are not intended for their benefit should be given a full explanation of the proposed procedure and the patient should feel free to withdraw from the tests at any time, says the committee. Except for trivial procedures of which venapuncture is an example, an explanation of the procedure should be given in the presence of a witness.

When the research is intended for the benefit of the patient the committee feels that there are circumstances in which it would be "inappropriate or even inhumane" to give detailed explanations of the procedures involved. Such cases should be investigated with particular care by the appropriate ethical committee.

SOVIET SCIENCE

Land and Sea

LUNOKHOD-2, which landed on January 16, 1973, in the Le Monnier crater on the eastern edge of Mare Serenitatis, had a region of particular selenological interest to explore—the transition from mare to highland. Operating among features assigned unofficial working names such as 'Head-on Hills', 'Shallow Crater', 'Round Bay', 'Near Cape', 'Far Cape' and 'Straight Rille', the Lunokhod recorded and transmitted data of considerable significance, not only to the interpretation of this specific type of area but to lunar research as a whole.

One of the most important experiments of Lunokhod-2 was the determination of possible changes in chemical composition of the transition area surface. A modified version of the RIFMA X-ray spectrograph used on Lunokhod-1 was used—the new instrument, RIFMA-M, being specifically adapted to determining the ratio of iron to other elements—notably aluminium and titanium. Near the landing site, on the slope of a crater of diameter 40 m, readings of Si, $24 \pm 4\%$; Ca, $8 \pm 1\%$; Fe, $6 \pm 0.6\%$; and Al, $9 \pm 1\%$ were obtained. (The iron reading obtained by Lunokhod-1 for Mare Imbrium was 10 to 12%.) As Lunokhod-2 moved southwards, towards the 'Head-on Hills' on the edge of the highland, no significant changes were at first observed—data from a 13 m diameter crater at approximately 1.5 km from the landing site were close to the first readings. But as it moved closer to the hills the iron content decreased and 5 km from the landing site it had fallen to $4.9 \pm 4\%$. On February 19 a minimum reading of $4.0 \pm 0.4\%$ was obtained. During this part of the survey, the aluminium content increased to $11.5 \pm 10\%$. Writing

in *Pravda* (November 20, 1973), Academician A. Vinogradov and Dr S. Solokhov attribute this change to a general variation in regolith composition in mare-to-highland transitions.

Panoramic television surveying of the transitional region revealed a number of interesting features, including a crater of diameter 15 to 20 m in the neighbourhood of the 'Head-on Hills' with associated slip terraces of some 10 to 15 m. In this region the density of small craters (diameter 2 to 3 m) fell to one half to one third of the average maria density.

A particular object of investigation was the 'Straight Rille', which stretches for some 15 to 16 km in a north-south direction along the south-east edge of Le Monnier. On both the eastern and western edges of the rille, a 30 to 40 m zone of intensive shear towards the fault was observed. The thickness of the regolith decreased as the lunokhod approached the rille and the lip consisted of a rock 'border' with boulders of diameter at least 1 to 2 m.

One interesting feature of the Lunokhod-2 programme was an attempt to correlate chemical composition to visual observation of the albedo. Using photometric telephotography from Earth and the RIFMA-M observations, a general relationship between the readings has been established. This is a result which is considered by the Soviet team to "extend considerably the significance of the Lunokhod-2 results".

The magnetometer experiments, a new feature of Lunokhod-2, revealed some characteristic variations in the field attributed to induction currents produced by variations in the interplanetary field. These data, it is claimed, should reveal the conductivity of the Moon to a depth of some hundreds of kilometres.

NUCLEAR WEAPONS

Poor Security

by our Washington Correspondent
LAST month, when fighting in the Middle East was at its peak, the United States Atomic Energy Commission (AEC) ordered security to be stepped up at all institutions which handle enriched uranium and plutonium, to ensure that none of the material could be stolen and end up as part of a nuclear finale to the Arab-Israeli conflict. The extra precautions were, it seems, more than justified, for a recent investigation by the General Accounting Office (GAO) has come up with the disturbing finding that security arrangements in some plants which hold strategic nuclear materials would pose few problems for a ham-fisted amateur burglar, let alone a terrorist organisation.

The most expensive, lengthy and difficult

cult part of making a nuclear weapon is the production of fissionable material, but fabrication of the weapon itself is reckoned to be a relatively easy task which would not be beyond the wit of scientists in most countries. Thus, if a supply of enriched uranium or plutonium could be diverted from installations in the United States, probably over a period of time, nuclear weapons could be within reach of those willing to pay the price. A crude bomb, such as the ones dropped on Hiroshima or Nagasaki, would require some 17 kg of enriched uranium or about 6 kg of plutonium, and it would, of course, take only one such bomb—or the threat of it—to upset the military balance in the Middle East.

The AEC itself acknowledged such risks in an internal report in 1971, which came to the conclusion that "as long as significant quantities of nuclear materials are in active use by the government, by government contractors, and by licensed commercial and other interests, there will be a distinct probability that some of those materials will be stolen, unexplainably or accidentally lost, diverted from authorised use, or used or disposed of in unauthorised ways".

With such considerations in mind the GAO, which carries out investigations for Congress, inspected the security arrangements in three plants which hold strategically important quantities of special nuclear material (as enriched uranium and plutonium are called). It found that in two of the plants, security "was so limited that protection was inadequate".

This is what the GAO found at one of the plants which, mercifully, remained nameless. The plant was protected by a part-time security officer and four armed guards, one of whom was on duty at all times, and it was surrounded by an 8-foot high wire fence. Special nuclear material, some of which is described in the report as being "of high strategic importance", was located in three buildings just inside the fence. Entrances to the building were connected to an alarm system.

On the face of things, that seems a fairly good security system, but the GAO found that it had the following defects:

- The fence had thirteen weaknesses, ranging from broken welds to inoperative locks, which would allow it to be breached with ease. Ten of the weaknesses were out of sight of the guard post.

- One of the storage areas was a prefabricated structure, just 16 foot from the fence, made from sheet steel panels 3 foot by 9 foot. According to the GAO investigators, who tested the strength of the panels with an adjustable spanner, "within 1 minute we were

one of the panels. At this point, the only impediment to entry was a small rivet which, in our opinion, could have been forced manually". Moreover, within 30 seconds, the investigators cut a 19-inch section of the panel with tin cutters.

- The door to the building could be opened easily because the lock had been broken, and it could be opened without activating the alarm.

- A second storage area could easily be entered through a vent in one of the walls. "With little effort", the GAO report states, "the louvres could be pulled out by hand and the inside screen could be manually forced, providing access to the building interior".

- Once inside the building, an intruder would have little difficulty in obtaining special nuclear material because it was stored in portable containers, which were "readily accessible". Moreover, plant personnel rarely entered the storage areas in the evening and night shifts, and the guards made regular rounds which could easily be monitored.

- Finally, all external means of communication at the plant were handled by a single cable, which entered the facility at a point which the guard could not see from his post. "Severing this cable would eliminate all means of timely communication with outside law enforcement agencies", the report notes.

The AEC says that it has taken steps to remedy the specific deficiencies outlined in the GAO report and earlier this year it issued a set of new regulations to tighten security at plants containing special nuclear materials. Nevertheless, the report does little to establish public confidence in the AEC's ability to keep an eye on its contractors and licensees, and it neatly underlines one of the arguments that critics of nuclear power have been persistently raising in the past few years.

It is frequently argued that proliferation of nuclear power plants will lead to an increase in the quantities of enriched uranium and plutonium in the United States, which will greatly increase the problems of ensuring that none of the material gets diverted into dangerous hands. At present, there are some ninety-five facilities in the United States which have at least 5 kg of weapons-grade nuclear material but by 1980 the AEC estimates that more than 1 million kg of special nuclear material will be required for the domestic power industry. Moreover, when the fast breeder reactor starts producing electricity in the 1980s, it will also start producing large quantities of plutonium. The extra precautions taken during the Middle East war will clearly be required on a longer term basis.

Short Notes

Crisis Under Control

STOPPING over in a power-reduced London on his way from a power-reduced Washington to a presumably warm Moscow, Dr Guyford Stever, director of the National Science Foundation and Science Adviser to President Nixon, paused long enough to tell a group of shivering journalists at the United States Embassy (where they take these things patriotically and the conference room central heating was down 20 degrees from the previous week) that the United States is going to more than double its expenditure on energy research over the next five years. A few years ago, Dr Stever said, about \$400 million was spent each year on energy research. This year it was between \$700 and \$800 million. Next year it would be \$1,000 million and over the next five years \$10,000 million.

Nonetheless, Dr Stever said, there will be a serious energy shortage in the United States for the next five years. The solution, he believes, lies in exploring coal liquefaction and gasification and in energy conservation. Fusion, he said, might be with us by the year 2000, although the enormous capital investment involved might make its progress slower than some people believe. Solar energy might also be making a contribution by then.

At any rate, the United States is determined as soon as possible to become completely independent of any other country for its energy. The Arabs, Dr Stever added, had precipitated the energy crisis in the United States but it was a problem that was coming anyway.

As for nuclear reactor safety, proper engineering and design can "easily handle" the problems. There is always a small danger, he said, but then no member of the public has ever been killed or seriously injured by an atomic accident in the United States.

Critical Difference

A row is brewing in the United States over just how severe the energy crisis is likely to be this winter. According to President Nixon and other Administration spokesmen, supplies of oil will be between 10 and 17% short of demand when averaged out across the country and the crisis, although severe, will not result in undue hardship. But according to a study carried out by the Library of Congress and published last week in the *Congressional Record*, the shortfall could reach a staggering 35% if the weather turns out to be unduly cold and if there is no relaxation of the Arab oil embargo. Moreover, even if the winter is relatively mild and Middle East oil starts flowing again soon, the

Library of Congress reckons that the gap between supply and demand will still be 20%.

The chief difference between the forecasts is that the Administration's sanguine predictions would probably not require rationing of petrol and heating oil, whereas the more pessimistic predictions of the Library of Congress almost certainly would. The disagreement is not, however, restricted to a battle of words between members of Congress and the Administration, for some of the President's own advisers are unhappy about the effects on public opinion if the Administration's reassurances turn out to be without foundation.

Australian Research

THE annual report of the Commonwealth Scientific and Industrial Research Organisation (CSIRO) of Australia for the year ending June 30, 1973, reveals that the total expenditure of the organisation increased by \$A6.17 million to \$A73.7 million during the year.

The report states that CSIRO is at present undergoing a significant re-orientation. In the past it has been "industry oriented" but it is now striving to become "people oriented". To achieve this aim the organisation is, for example, changing the tone of its environmental research so that its relevance to industry is "more tenuous".

With this change of emphasis the report states that there is a need for a more effective communication "with the community as a whole". The organisation is taking steps to meet these needs but gives no details of the procedures involved.

Nixon's Economy

SOON after exhorting all Americans to conserve energy to help stave off a potential crisis this winter, President Nixon boarded his presidential airliner for a weekend trip to Florida. According to the White House, the return journey used up 8,000 gallons of fuel. According to the *Washington Post*, which is not one of Mr Nixon's most ardent admirers, that amount of fuel would have allowed one commuter to travel from the outskirts of Washington to his office and back every day for 11 years. Mr Nixon did, however, order the pilot of his aircraft to slow down to 475 miles an hour, thus saving 200 gallons of fuel an hour.

Mars for 10p

A 'street astronomer' has been spotted in London's Shaftesbury Avenue. Armed with a 75-mm telescope and sky maps, he offers passers-by a view of Mars for 10p (*Junior Astronomical Society Circular*, No. 57; November 1973).

NEWS AND VIEWS

Role of Sex-linked Histocompatibility Antigens

CURRENT interest in histocompatibility antigens, apart from technical problems concerning their investigation and practical problems connected with transplantation in man, largely centres on their biological role. As has been frequently pointed out, it is difficult to believe that such a major genetic investment has no biological importance. Differing views on the biological role of the major histocompatibility locus in any species, including HL-A in man and H-2 in mice, have been expressed, ranging from those who see them as connected in some way with the generation of immunoglobulin gene diversity, and those who consider that their function is concerned with the maintenance of the integrity of the individual, being involved in protection either against neoplasms or against the potential invasive problems which accompany the evolution of viviparity. These views have recently been discussed in the pages of *Nature* by Bodmer (237, 139; 1972) and Burnet (245, 359; 1973).

It is also legitimate to ask, however, whether the 'minor' histocompatibility loci, and indeed other antigenic polymorphisms such as the ABO blood group system in man, also play a part in the functions suggested for the major histocompatibility locus. Some of the minor loci in the mouse, the only species studied in any detail, seem to be almost as complex as H-2, and once again it would be good to think that such a major genetic investment supposes some biological function. Is this function a modification or elaboration of the functions of the major locus, or do the minor loci have some distinct part to play?

If such questions become puzzling for the minor autosomal loci, they become positively bewildering when related to X and Y-linked histocompatibility antigens. Whatever the significance of histocompatibility loci in general, X and Y-linked H loci are clearly a very special case, and many of the possible functions of autosomal loci clearly cannot be carried out by sex-linked loci. There is much less hard information about the X and Y-linked antigens, partly because of the technical problems of their investigation. Recently considerable advances in knowledge of one such system, the H-Y antigen in the mouse, have been made, stemming from the technical advances in detection of H-Y antigens made by Boyse and his colleagues.

The results of one such study by Bennett and Boyse are reported on page 308 of this issue of *Nature*. They reinvestigated the question of whether immunisation against H-Y antigens in female mice might alter the sex ratio in their progeny. They remind readers that such investigations have been conducted before, but always by attempting to immunise the female *in vivo*, and that such investigations have always been negative or equivocal, but that it was previously impossible to decide which of the many possible reasons for this failure to demonstrate immunoselection was correct. They exposed sperm to anti-H-Y and complement *in vitro*, and then artificially inseminated females, and did indeed show a small but statistically significant decrease in the proportion of male offspring in litters of such females.

Bennett and Boyse discuss, in an admirably cautious way, the conclusions to be drawn from their observations. Two points may be emphasised. One is that this is some evidence that the H-Y gene may be concerned with the sex ratio, a conclusion which one would hesitate to make *a priori* when one considers the ragbag of genes known to be present on the sex chromosomes. The other point that should be stressed is that although the alteration in the sex ratio observed is small, and complete elimination of male offspring was not achieved, the alteration in the sex ratio was from 53% males in untreated litters to 45% in experimental litters, that is, an increase of 8% in the proportion of females. Although small, one can imagine many situations in farm livestock where such a change, if accompanied by no decrease in fertility, would be of considerable economic importance.

From a Correspondent

Hot Spots Must Move

If linear chains of volcanoes in the ocean basins originate as outflows from localised regions near the Earth's surface—hot spots—over which plates have moved during geological times, then these hot spots cannot have formed a fixed frame of reference during the past 40 million years. This is the conclusion of Molnar and Atwater in this issue of *Nature* (page 288). This result has major implications for the hot spot hypothesis as there has up to now been a hope among geophysicists that hot spots might have been semi-permanent features and thus good markers of absolute motion of plates over the mantle. The implications, however, go beyond the geometry. If hot spots are not stationary relative to each other, there are serious questions to be asked about their physical character and how it permits them to migrate.

Since the idea of very active volcanic sources leaving their trace on plates was revived by Morgan three years ago, many groups have attempted to use the concept to learn more about past motions. The results have been strangely inconclusive. The one undeniable thing from the geological and geophysical evidence is that the long traces ending in present day volcanoes do indicate something other than pure chance. Many geophysicists would further agree that there is something global to the traces—they are not ten or so entirely unrelated phenomena. But beyond there, opinions differ. Are hot spots simply localised lava sources, or do they have any vertical extension? Are the traces markers of pre-existing fractures or can hot spots punch volcanoes in unfractured plate? Present day geometry of the traces, palaeomagnetic data and a reasonable understanding of plate positions for the past 70 million years are all one has to go by at the moment.

Hargraves and Duncan (*Nature*, 245, 361; 1973) analysed palaeomagnetic data and concluded that they were inconsistent with hot spots being stationary relative

to the Earth's magnetic field. Since there are reasonably strong grounds now for assuming that the pole does not wander, it was necessary to assume that the hot spots do. Hargraves and Duncan were able, however, to find a rotation of the mantle as a whole which reproduced their results tolerably well without the need for the migration of individual hot spots. There is thus the possibility that not only do plates move, but the material that they slide over is also in motion.

Molnar and Atwater adopt a geometrical approach which does not use palaeomagnetic evidence directly. They use the now generally agreed upon poles of rotation of plates to run the geological clock back 38 million years. They place the 38 million-year-old rocks on the Hawaiian chain over the present position of the Hawaiian hot spot and see what overlay the other hot spots at that time. None of the linear features lies on top of their presumed parental hot spots when this analysis is carried out. This implies that there must have been relative motion among hot spots in the past.

It is now necessary for geophysicists to consider these two papers very carefully. The authors do not come to identical conclusions, but this is perhaps not surprising. What they do point to fairly clearly is some sort of mobility below the lithosphere—a mobility of up to a couple of centimetres a year. How deep this mobility extends there is as yet no idea, and although it is still possible that the Morgan hypothesis that hot spots are fed by deep mantle plumes is tenable, there are now very serious doubts that such a delightfully simple model can apply. Yet more solid ground of nature is eroded. D. D.

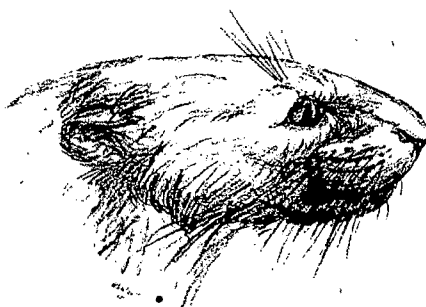
SYSTEMATIC ZOOLOGY

Bearish Carnivores

from our

Vértebrate Palaeontology Correspondent

THE seals, sealions and walruses are normally separated from all other members of the Carnivora by being placed together in a suborder Pinnipedia. It is generally agreed that the pinnipeds are more closely related to the canoid than to the feloid carnivores, and the implication of their placement in a separate suborder is that they all had a common ancestry within the Canoidea. For some time, however, several workers have considered it likely that the otariids (sealions and walruses) whose hind limbs project backwards, and the



Artist's conception of head of *Enaliarctos*.

phocids (fur seals) which can bring their hind limbs forwards beneath the body, originated from different groups of canoids. These workers believed that the otariids were derived from bear-like canoids, whereas the phocids had evolved from otter-like canoids.

Important new evidence on pinnipede origins has been published by Mitchell and Tedford (*Bull. Am. Mus. nat. Hist.*, 151, 201; 1973), who describe a new early Miocene aquatic carnivore whose skull and dentition are morphologically intermediate between those of terrestrial ursid canoids and those of aquatic otariid pinnipeds.

The new otariid, *Enaliarctos*, is placed in its own new subfamily. Its similarities with the canoids include features of the auditory region which are fundamental in the classification of the Carnivora. This region of *Enaliarctos* is similar to that of early, Oligocene members of the Canoidea, but in several ways is most similar to that of primitive ursids, and to that of the late Oligocene aquatic form *Potamotherium*. (*Potamotherium* has previously been regarded as itself related to the late Cainozoic otters, but Mitchell and Tedford believe that it was already too specialised for aquatic life to be ancestral to them.)

Enaliarctos is also similar to ursids in having retained two quadrangular upper molars, and in the structure of its upper and lower fourth premolars. A natural cranial endocast also shows traces of the 'ursine lozenge' on the antero-dorsal surface of the cerebrum. On the other hand, the skull of *Enaliarctos* shows several similarities to that of otariid (rather than phocid) pinnipeds, and its dentition shows a stage intermediate between that of the primitive ursids and the reduced, simplified pinnipede dentition. Features which suggest an aquatic life include its broadened muzzle and enlarged narial chamber, large dorsally placed eyes and enhanced cranial blood circulation. *Enaliarctos* was also found in marine, near-shore deposits.

Mitchell and Tedford conclude that *Enaliarctos* was closely involved in the ancestry of the Otariidae, and place it in that family. Its similarity to ursids, therefore, leads them to place the Otariidae with its terrestrial relatives

within the superfamily Canoidea, adjacent to the Ursidae. They believe that they have demonstrated a sequence from primitive ursids to otariids that leaves little room for origin of the phocids. The earliest phocids are, like *Enaliarctos*, of early Miocene age. Unless they evolved from a stock closely related to the ancestors of *Enaliarctos*, but already committed in a divergent fashion to an aquatic way of life, there seems little doubt that the phocids are a lineage separate from the otariids. If so, the Pinnipedia is a diphyletic group, and the terms Pinnipedia and Fissipedia should no longer be used.

The Ursidae has also been enlarged recently by Sarich (*Nature*, 245, 218; 1973), whose immunological studies of the pandas have supported the earlier work of Davis (*Fieldiana, Zool. Mem.*, 3; 1964) in showing that the giant panda and the lesser panda are not closely related to one another. Instead, the giant panda is merely a highly specialised type of bear. The ursids and procyonids (raccoons) are more closely related to one another than to any other canoid. The lesser panda seems to have a separate lineage originating from near the common ancestry of these two families, though perhaps more closely allied to the ursids than to the procyonids. Sarich's immunological studies also support the morphological studies in emphasising the comparatively conservative nature of the Ursidae.

CYCLIC AMP

Regulator of Cell Shape

from a Correspondent

THE proliferation of papers implicating cyclic AMP (3',5'-adenosine monophosphate) as a growth regulator in animal cells is now well into the exponential phase, and even those working in the field may feel justifiably overwhelmed by the amount of new data. Moreover, much of this information is concerned with correlating changes in the behaviour of cells with changes in intracellular cyclic AMP concentrations following relatively complex manipulations, such as exposure to serum or transformation by oncogenic viruses. As more becomes known about possible interactions between different elements of the cyclic nucleotide pathways—for example, the induction of phosphodiesterase by its substrate cyclic AMP and the stimulation of at least one cyclic AMP phosphodiesterase by cyclic GMP—the problem of sorting out exactly where these complex stimuli initially interact with the cell's regulatory programme is greatly increased.

This task would be much easier if it were possible to predict the consequences of selectively altering only one

of the many variables. One way to do this is to isolate temperature sensitive mutants of the different proteins involved in cyclic nucleotide metabolism and the preliminary results of such an approach are described by Willingham, Carchman and Pastan (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 2906; 1973). In order to select for mutants of cyclic AMP metabolism Willingham *et al.* made use of the fact that high levels of this nucleotide enhance the adhesiveness of mouse 3T3 cells to plastic. Cells with low amounts of cyclic AMP would therefore be expected to round up and lose contact with the substratum, and this behaviour was observed in one clone of mutagenised cells, after shifting them from 39° to 23° C. The change occurred within 5 min and disappeared after a few hours at the new temperature, when the cells spread out and re-attached to the dish. This behaviour correlated very neatly with changes in cyclic AMP inside the cells; 2 min after the temperature shift cyclic AMP was at a minimum, but it soon increased and by 2 h reached concentrations up to five times greater than in control cells before declining. Immediately after the temperature change the mutant cells released cyclic AMP into the medium and this, at least in part, accounts for the drop in intracellular cyclic AMP.

Inter alia Willingham *et al.* also observed granular deposits on the dishes in which the mutant cells had been grown for several days. Electron microscope pictures revealed that cell processes were attached to these deposits rather than directly to the plastic but, apart from showing that they contain some protein, the authors were not able to account for this strange phenomenon. The site of the *ts* mutation in these cells has not yet been identified, though adenylate cyclase and phosphodiesterase appear normal. Somewhat surprisingly the transient change in adhesiveness was seen when cells were shifted either up or down in temperature, and there seemed to be no critical temperature at which the cells responded, suggesting that the mutation may not be as straightforward as one would like.

Animal cells with inheritable differences in cyclic AMP metabolism have also been studied by Gilman and Minna, in two papers in a recent issue of the *Journal of Biological Chemistry* (248, 6610; 1973). Rather than isolating mutants in the manner of Willingham *et al.*, they surveyed a variety of already existing rat and mouse cell lines for their ability to respond to catecholamines and prostaglandins with an increase in intracellular cyclic AMP. Cells were classified as either β^+ or β^- (responders and non-responders to β -adrenergic stimulators) or P^+ or P^- (responders and non-responders to

prostaglandin E_2). Hybrids made between β^+ and β^- cells were all β^- , at a time when almost all the parental chromosomes were still present, whereas similar hybrids between P^+ and P^- cells were all P^+ . It is tempting to assume that the phenotypes β^+ and P^+ are associated with the presence of receptor proteins in the plasma membrane which are capable of activating adenylate cyclase, but it remains to be seen why the regulation of expression of the two phenotypes is so different.

MEDICAL GENETICS

Penrose Honoured

from a Correspondent

A SYMPOSIUM to commemorate Lionel Penrose, who died suddenly last year during a retirement which had curtailed neither the breadth of his curiosity nor the practical application of his experience to the problems of mental defectives and their relatives, was held in London on November 16 and 17 during the 173rd meeting of the Genetic Society.

The first session was chaired by the President of the Royal College of Physicians, C. A. Clark, who pointed out that Penrose was the first medically qualified holder of the Galton Chair. The session was then introduced by B. Childs (Johns Hopkins University, Baltimore) who exhibited the direct and elegant approaches he is using in the study of patients who have specific difficulties in reading, and was even able to supplement the message of his slides by

exploiting the technical difficulties due to the screen being smaller than the slide image. J. H. Edwards (Birmingham Maternity Hospital) then spoke of the difficulties implicit in the disjunctive use of monogenic and polygenic in observational genetics and the alternative approach of estimating the frequency and strength of the most powerful allele present.

E. T. O. Slater (Institute of Psychiatry, London) then spoke on the hereditary dementias of adult life, with special reference to Huntington's chorea, a condition in which the heterozygote cannot yet be identified in the interval between fertility and morbidity, and sporadic cases cannot be diagnosed with precision. In the final paper of the session, C. A. B. Smith (Galton Laboratory, University College, London) explored yet another of Penrose's interests with yet another parameter defining gametic correlations, this time with the remarkable property that the series of related constants are further related by simple but unusual numerical operations on their subscripts. The final paradox seemed to imply that, so far as gametic correlations are concerned, where, as well as with whom, our ancestors lived may have contributed appreciably to conventional measures of inbreeding.

The next session, which appropriately dominated the meeting, was a video tape presentation by J. Cohen and L. J. Lawler (University of Manchester) and by R. Penrose (University of Oxford), one of Lionel Penrose's three sons. After an introduction of Penrose's works in pencil, woodcut and oil, and

Interaction of tRNA with 5S Ribosomal RNA

SEVERAL years ago it was suggested that the 5S RNA of the 50S ribosomal subunit is important for transfer RNA-ribosome binding. In particular, it was recognised that the sequence UpGpApApCp of 5S RNA could interact with the T ψ C loop of tRNA. Evidence has since been accumulating to support this hypothesis; first, it has been shown that the fragment Tp ψ pCpGp specifically binds to a 5S RNA-protein complex; second, non-enzymatic binding of aminoacyl tRNA is inhibited by the same fragment; and, third, two adenines of 5S RNA, which are essential for biological activity and the binding of Tp ψ pCpGp to the 5S RNA-protein complex, are on the surface of the ribosome.

To decide the possible biological significance of these data, Richter, Erdmann and Sprinzl studied the effects of the tetranucleotide (T ψ CG) on tRNA dependent reactions, and they report their results in *Nature New Biology* next Wednesday (December 5). They

found that when the oligonucleotide binds to the 50S ribosomal subunit it inhibits elongation factor (EF)-Tu-directed aminoacyl-tRNA binding, and EF-Tu-linked GTP hydrolysis and ribosome-dependent synthesis of 'magic spot' I. The anticodon loop and the CGA end of tRNA molecules have already been shown to function in protein synthesis. These results show that the T ψ C loop is almost certainly also involved.

As further evidence the authors note that in a recently proposed three-dimensional model of yeast tRNA^{phe}, the Tp ψ pCp is on the surface allowing it, theoretically, to interact with ribosomes, and also that equilibrium dialysis experiments have shown that the T ψ C loop is not base-paired in solution. Although convinced that the oligonucleotide Tp ψ pCp of tRNA binds to ribosomes, the authors are not completely certain that the binding site is on the 5S RNA and intend to investigate this matter further.

the sight, though not the sound, of a remarkable musical composition, complete with semitones, in which the second half was played by inverting the score of the first half, Roger Penrose exhibited an extraordinary series of wooden objects extending from solid representation of impossible objects to relatively simple two-dimensional sliding or slotting puzzles. He ended with a series of self-duplicating objects from the original rhombi demonstrated at the International Genetics Meeting in 1958 in Montreal to self-replicating and self-separating chains of differing units. The remarkable nature of these artefacts was made even more impressive by the manual dexterity of the demonstrator and the depth and lucidity of his commentary. Copies of this tape are available through Professor Cohen (Department of Psychology, University of Manchester).

The symposium continued the next morning, under the chairmanship of J. H. Renwick, with a historical survey and an up-to-date review of the linkage relations of the human red cell groups by R. R. Race (Lister Institute, London). This form of analysis was largely dependent on the work of the Galton Laboratory (under the serial triumvirate of Fisher, Penrose and Harris) where much of the analytical and enzymatic work was developed, and of Race's laboratory at the Lister which provided much of the data, and undertook, by hand, many of the analyses at a speed which defeated the computer. These reviews were followed by R. Ceppellini (University of Turin) who spoke on the linkage relationship of the white cell surface determinants which, unlike those known on the red cell, are defined by several determinants arranged over a segment one or two centimorgans long.

The symposium finished with the Penrose Memorial Lecture, given by Penrose's successor Professor Harry Harris who explored allelic variation in man and reviewed the work of his own laboratory, on electrophoretic evidence of functional enzymatic variants, and related to this data from the mapping of man's best-known protein unit of haemoglobin, the beta chain and data on the frequency of those functionless or silent alleles which can be defined by neonatal screening for aminoacidurias.

It was appropriate that a man whose main influence was to expose his own species to the standard of professional scrutiny and objective accountancy established in the genetical study of his parasites, and of his edible and ornamental plants and animals, should be commemorated by a final session in which man was established as the leader, with his own blood, in the objective auditing of claims of selection and chance or, as Kimura might have it, of drift and drive.

HORMONES

Diabetes Control

from a Correspondent

THE role of insulin in the control of plasma glucose concentrations is well known. More recently, the protein hormone glucagon has also been implicated. It has been found that diabetic subjects with high plasma glucose (hyperglycaemia) not only have lower levels of effective insulin activity but also have increased plasma glucagon compared with normal subjects. This may occur because the hyperglycaemic suppression of glucagon release requires insulin. Diabetes is thus a bihormonal disease. Both hormones seem to regulate plasma glucose by their action on the liver, where they are known to have opposite effects on the synthesis and degradation of stored glycogen.

One of the mechanisms by which these hormones exert their opposing actions in liver cells is by stimulation or inhibition of membrane-bound adenylyl cyclase, the enzyme which regulates the intracellular concentration of cyclic AMP (Illiano and Cuatrecasas, *Science, N.Y.*, 175, 906; 1972). Thus it would seem that a decrease in plasma glucagon in a diabetic subject might offset the effect of the lower insulin level. Because glucagon is a protein hormone, one method of depressing its effect would be to produce antibodies against it.

This possibility has now been tested by Epand and Douglas working with immunised rabbits (*Biochem. biophys. Acta*, 320, 741; 1973). Although bovine, porcine, rat, human and rabbit glucagons are known to be chemically identical, rabbits are still able to produce antibodies to bovine glucagon when the latter is mixed with a suitable adjuvant before injection. Epand and Douglas reasoned that as glucagon is known to stimulate the release of insulin, rabbits whose effective glucagon concentration is decreased by the presence of specific antibodies should have a correspondingly decreased concentration of insulin. Because of the antagonistic effects of the two hormones the resulting concentration of blood glucose should be similar to normal.

To test their theory Epand and Douglas compared the plasma glucose, insulin, and glucagon antibody levels of rabbits immunised with glucagon injections for 4 weeks, with control animals. All the experimental animals produced antibodies to glucagon, but none to insulin. The glucose concentrations in plasma samples of experimental and control animals were virtually the same. The insulin levels of the immunised group of animals, however, were less than half those of the non-immunised rabbits. These results suggest strongly that the presence of glucagon antibodies in immunised rabbits

renders them able to maintain normal blood sugar concentrations with a reduced level of plasma insulin. It is thus likely that the presence of glucagon antibodies lowers the concentration of active glucagon in the plasma which, in turn, decreases the secretion of insulin. The combined reduction of the concentrations of the two antagonistic hormones has little effect on blood glucose.

Epand and Douglas also show that immune rabbits can use administered glucose as quickly as the control rabbits in the glucose tolerance test, but without as great an increase in plasma insulin. The production of glucagon antibodies in a human subject has been reported (Stahl *et al.*, *Horm. Metab. Res.*, 4, 224; 1972). These results therefore suggest a potential use for glucagon antigenicity in diabetic therapy. Less insulin would be required to maintain normal blood glucose levels of a diabetic patient who has been immunised with glucagon antibodies.

PEST CONTROL

Attack on Rodents

from a Correspondent

RODENT pests are most effectively controlled with poisons. Such rodenticidal agents are hazardous, their biological actions are by no means specific for the target species, and their use presents a danger to both man and domestic animals. New approaches to the problem of rodent control, by chemosterilisation and genetic means, are discussed by Marsh and Howard in a recent issue of the *Bulletin of the World Health Organisation* (48, 309; 1973). Chemosterilisation has reached the experimental stage of development, whereas the genetic approach is still highly speculative.

The eventual application of both lines of attack will mean, except in instances where an immediate and complete disappearance of pests is required, a gradual and a biologically far sounder depletion of rodent populations than is possible with present methods of control. This steady and more natural dilution of a rodent population density may, depending on the situation, be advantageous, of no consequence or disadvantageous. In instances of rodent-borne diseases a steady decline in numbers would be advantageous; there would be no sudden appearance of disease vectors from poisoned rodents as would occur in the case of a sudden drop in numbers resulting from the use of rodenticides. In areas such as rangeland, crop-producing areas, sewers and warehouses, where complete eradication of pests is not necessary, chemosterilisation and genetic control measures will be entirely satisfactory. And in cases where use of the rapidly effective rodenticides is necessary, chemosterilisa-

tion and genetic measures will form an important means of consolidating such eradication and keeping at bay the incipient resurgence of the suppressed rodent population.

Chemosterilisation is a term broadly used to include direct effects (either permanent or temporary) on the fertility of either or both sexes, and indirect effects (through behavioural or physiological mechanisms) on the reproductive capacity of the population or on the fecundity of the offspring.

A number of compounds—chemicals that can be administered directly to the natural pest population in baits and tracking dusts—have been evaluated for use as potential chemosterilants. The practicability of using hormonal compounds in this manner to inhibit the development of embryos is reduced because such compounds have to be made available throughout the breeding season. Alkylating agents are currently showing greater potential for use as chemosterilants. These compounds possess a wider range of biological activity than hormones because they affect the fertility of both sexes at adult or progenitive stages. One of the most promising agents is 3-chloro-1,2-propanediol, a compound which creates permanent sterility in certain rodent species and causes temporary sterility in a rather wider variety of mammals. The specificity of such anti-fertility agents would minimise any risk to humans and domestic animals.

Means of effecting chemosterilisation indirectly are suggested by Marsh and Howard. These include inhibiting the production of sexual pheromones so upsetting normal reproductive behaviour, and increasing the fertility of rodent pests so overloading the population and causing it to crash (as occurs naturally in some species).

The genetic approach to rodent control is at present theoretical, and though feasible is, practically, far from simple. Genetical factors are required that will make the population inherently more susceptible to diseases, to predation, to intraspecific stresses, to imbalances in physiological and behavioural processes and to its own lethal genes. Such genetical traits, introduced into the natural population by the release of new breeding stock (reared in captivity), will be diluted out of the population unless they possess a selective advantage also. The frequency with which fresh breeding stock would need to be introduced into the natural populations remains to be determined. Genetical changes could be induced directly in the natural pest populations by exposure to suitable mutagenic compounds. These, however, would be shorter-acting and less specific than genetical control by inheritance.

Rodent control measures, when designed in accordance with these pro-

posals, will provide a benign means of attacking the problem of rodent pests as compared with the current use of poisons. One great advantage is that control will be highly selective, particularly in the case of genetic control where procedures can be aimed directly and specifically at a particular pest population. And in the case of the genetical approach the control measures may also be self-perpetuating.

NEUROCHEMISTRY

Strychnine Binding

from a Correspondent

STRYCHNINE is not perhaps the most subtle of drugs. Sensible persons would do better to inquire among the more obscure members of the South American Crotalidae or Elapidae for poisons acting with rather less striking manifestations.

Nevertheless strychnine, in spite of its shortcomings, has had a most distinguished scientific career in modern times as in old. Elucidation of its structure—one of the great classics of structural organic chemistry—was engineered 30 years ago by Robert Robinson. R. B. Woodward, in one of those thoroughbred total syntheses that appear from time to time out of Harvard, put together what Robinson called "for its size the most complex substance known"—he was biased but probably correct. The establishment of the absolute configuration by X-ray crystallography came in the mid nine-

teen fifties. Everything about strychnine seemed solved therefore, except precisely how it acts in the nervous system. But this seems to be a mystery no longer.

In the latest issue of the *Proceedings of the National Academy of Sciences* (70, 2832; 1973) Young and Snyder describe their use of tritiated strychnine to measure the binding of the poison to synaptic membranes. It has been known for many years that strychnine antagonises synaptic inhibition, especially in the spinal cord. Young and Snyder now report that one reasonable prerequisite for the effect can be demonstrated; that is to say, they have found a specific interaction of strychnine with synaptic membranes of rat spinal cord. Specific binding was about eight times greater in purified synaptosomal fractions or synaptic membranes than in the starting homogenate and was found to be saturable with half-maximal binding occurring at about 3×10^{-8} M. The rate of interaction of tritiated strychnine with purified synaptic membranes is remarkably fast: binding is maximal within a minute at 25° C and even at 4° C half maximal binding takes just 36 s. The rate of dissociation of the complex by excess cold strychnine is unmeasurable at 25° C: at 4° C the half life is estimated as about 30 s. The dissociation constant from these measures gives a high value of about 4×10^9 M for a single species of strychnine receptor.

Synaptic inhibition in spinal cord and brain stem (but not in cerebral cortex) is brought about by glycine, the simplest of amino acids. Glycine is a major inhibitory neurotransmitter in the cen-

Endonuclease Recognition Site Sequenced

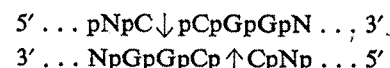
It seems certain that the process of bacterial restriction is mediated by endonucleases which recognise particular sequences in 'foreign' DNA. The sequences recognised by endonuclease R from *Haemophilus influenzae* and by endonuclease RI from *Escherichia coli* have been determined, and in *Nature New Biology* next Wednesday (December 5) Sugisaka and Takanami report the analysis of the sequence recognised by *Haemophilus aphrophilus* endonuclease (endo AP).

To demonstrate the specificity of the enzyme it was necessary to show that it degrades different DNAs in the same way. In these experiments T3 DNA and fd RFI (doubly closed replicative form) DNA were degraded with endo AP and sequence analysis of the 5' and 3' ends of the fragments gave identical results for both DNAs.

After degradation of the DNAs with endo AP the 5' ends were labelled with ^{32} P using polynucleotide kinase (after alkaline phosphatase treatment). The sequence at all these 5' ends was shown to be pNpCpGpCp (N = A, G, C or T).

To determine the 3' end of the fragments both DNAs were uniformly labelled with ^{32} P *in vivo* then digested with endo AP. Following hydrolysis with micrococcal nuclease the NpN fraction from the 3' ends was analysed. The 3' ends of these dinucleotides all had the sequence—pNpC.

Using the information on both the 3' and 5' terminal nucleotide sequences, the authors conclude that the sequence recognised by endo AP must be:



The arrows indicate the point of cleavage.

Endo AP cleaves the fd RFI DNA at thirteen sites yielding fragments of about 500 base pairs. If the base sequence is random the sequence CCGG would be expected to occur once in every 625 nucleotide pairs. It therefore seems likely that the sequence of tetranucleotide pairs contains enough information to account for the observed degree of specificity.

tral nervous system and strychnine antagonises the hyperpolarising effects of glycine at spinal synapses. One plausible mechanism for the antagonism turns out to be correct; strychnine and glycine compete for the same synaptosomal binding sites. This is shown by dissociation of the tritiated strychnine-synaptic membrane complex by a large excess of cold glycine. The affinity of glycine for the specific receptors is three orders less than that of strychnine which fits in with the neurophysiological evidence for the dominance of strychnine over glycine.

Another piece of evidence supporting this contention is the almost identical regional distribution of endogenous glycine levels in the central nervous system—low in brain, medium in brain stem and highest in spinal cord, with the increasing capacity of synaptosomal fractions obtained from these regions to bind strychnine. It should therefore now be possible to pull out and identify the membrane components responsible for strychnine binding in the central nervous system and to compare these with the high affinity sites responsible for glycine uptake in nerve terminals that seem not to bind to strychnine.

MOOSE

Sodium Requirements

from our Plant Ecology Correspondent

SODIUM is an element which is required in far greater proportions by animals than by plants; in general plants tend to accumulate potassium from their environment rather than sodium. Since herbivorous animals rely on plants to a considerable extent for their ionic requirements, it is possible that in certain circumstances vegetation will fail to meet the sodium requirement of its herbivore predators.

This is precisely the situation which is described by Botkin, Jordan, Dominiski, Lowendorf and Hutchinson (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 2745; 1973) on the Isle Royale National Park, Lake Superior, Canada. In this isolated and undisturbed ecosystem, an equilibrium exists between the vegetation, the moose population and their predators the wolves. It is estimated that 1,000–1,200 moose occupy the 550 km² of mixed conifer and deciduous forest of the Isle Royale Park, but in spite of this very high population density there is no evidence of sodium deficiency among the animals. This is surprising, since the bulk of the food of the moose consists of the current year's growth of leaves and twigs of woody plants, which are shown by Botkin *et al.* to contain little sodium.

An annual total of 170 kg of sodium in the material suitable for moose consumption in Isle Royale was estimated

assuming a concentration of 10 p.p.m. within the browsed material. This assumption is not unreasonable; for example, determinations for sodium concentration in leaves gave *Abies* 2.8 p.p.m., *Betula* 15.8 p.p.m. and *Populus* 7 p.p.m. Allowing for the fact that only 10–20% of the available browse is removed, the total sodium input from this source into the moose population is 17–34 kg yr⁻¹. But it would seem, from calculations of the sodium content of new tissues minus sodium losses from the urine and faeces of the moose, that the population in Isle Royale has an intake of 243 kg yr⁻¹. The browsing of moose, which represents 90% of the animals' annual food intake, thus supplies only 7–14% of its annual requirement for sodium.

The question arising from these data is where do the moose obtain the balance of this requirement? One possibility is that the animals derive their sodium from the mud licks which they are known to use, but this is unlikely because these licks contain concentrations of only about 24 p.p.m. sodium, a value only twice as great as most of the leaf material.

During a period of about 8 weeks in the summer, moose feed extensively on aquatic plants which were found to contain very high concentrations of sodium: for example, some of the

by Botkin *et al.* were *Calla palustris* 1,713 p.p.m. of sodium, *Carex rostrata* 246 p.p.m., *Myriophyllum* 4,750 p.p.m. and *Utricularia* 8,048 p.p.m. These values are between twenty and eighty times greater than those obtained for terrestrial vegetation, and are greater in floating and submerged aquatics than in emergent species.

Calculations from the productivity of these aquatics show that some 2,500 kg sodium—ten times the annual requirement of the herd—is available for moose consumption each year in the park. Although this may account for the overall annual sodium budget, it does assume some mechanism for sodium retention in the moose during the 10 months of the year when sodium is scarce. The authors suggest that potassium may be substituted for sodium in certain circumstances, for example in parotid secretions, which would result in sodium conservation.

MICROEARTHQUAKES

Earth Tide Trigger

from our Geomagnetism Correspondent

ALTHOUGH there have been many attempts to show that tectonic and volcanic activity can be triggered by other much smaller forces, few have been entirely convincing. Moreover, this is a field in which apparently valid claims to have detected correlations are

often shot down shortly after by equally, if not more, convincing explanations of the same data. One therefore tends to approach such claims warily, holding back any jubilation until other workers with similar interests have had time to make up their own minds. Having said that, however, there certainly seems to be something in a demonstration by Mauk and Kienle (*Science*, N.Y., **182**, 387; 1973) that certain microearthquakes in Alaska are triggered by Earth tides.

This is not the first time that Earth tides have been proposed as trigger forces, although again there is a long record of failure to produce convincing evidence. Mauk and Kienle believe that the correlation between microearthquakes in an aftershock sequence and the principal diurnal tidal component, found by Ryall *et al.* (*Bull. seism. Soc. Am.*, **58**, 215; 1968), may be the one success as far as earthquakes are concerned; and Johnston and Mauk (*Nature*, **239**, 266; 1972) have reported a "definite" correlation between the eruption periodicity of Stromboli and the fortnightly tidal component. But apart from these and one or two other possible correlations involving volcanic activity there is very little else—a general failure which Mauk and Kienle think reflects not that Earth tides cannot act as trigger forces, but rather that, if they are to do so, three strict conditions must be satisfied.

The first of these is that the level of tectonic stress in the area must be high enough initially, and that the rate of accumulation of tectonic stress must be "sufficiently smaller than the periodicity of the tides", for the small-amplitude tidal perturbations to have an effect. Second, events must be closely grouped in space for there to be the chance of having a spatially homogeneous mechanism able to respond to the perturbations and thus trigger each event in a similar way. And, finally, events must be shallow enough to lie in regions where brittle fracture of the rock is important.

Each of these conditions is thought to apply to both aftershock zones and volcanic regions, and thus particularly to St Augustine volcano which has been investigated by Mauk and Kienle. St Augustine, which lies at the mouth of Cook Inlet in the Aleutian Islands, is an active composite volcano comprising an alternating series of outward-dipping pyroclastics and andesitic and dacitic lava flows and a central endogenous lava dome. Seismic monitoring since 1970 has indicated considerable microearthquake swarm activity during which the number of events per day may rise two or three orders of magnitude above the background level. That the shocks have extremely shallow foci is shown, first, by the determinations of focal positions, and Mauk and Kienle suggest

that the origin of the events may be related to deformation and fracturing occurring during periods of rapid growth of the central volcanic cone. Moreover, with one exception, for which $b = 1.35$, the b values for the eight swarms analysed ranged from 1.7 to 2.5. This again supports the idea that the events are shallow in that Minakami (*Bull. Earthq. Res. Inst.*, **38**, 497; 1960) has shown that high (2–3) b values arise from earthquake swarms originating at depths of generally less than 1 km. In addition, shallow origins of the shocks may be deduced from the body wave attenuation patterns.

Plots of the hourly frequency of the microearthquakes generally show a diurnal peaking of activity which, for the seven high b value swarms, correlates visually with peaks in the calculated magnitude of the total tidal vector. Two distinct phase relationships were observed, however, each occurring with roughly the same frequency. The slightly more frequent phase relationship involved no obvious phase shift between the earthquake activity peaks and the corresponding tidal vector peaks when observed visually, although detailed statistical analysis more accurately indicated a phase shift of about one hour with the peak microearthquake activity lagging the tidal peaks. The slightly less frequent phase relationship involved a visual lag of 5–6 h (about 5 h from detailed analysis) for the microearthquake activity. As far as the one low b value swarm was concerned, no visual correlation was apparent. Detailed statistical correlation showed, however, that the phase lag of 1 h was present here also, albeit with a higher standard deviation than for the other swarms.

The swarms investigated occurred during 1971 either before or after the volcanic eruption of October 7, 1971, but no differences in the temporal variations between pre-eruption or post-eruption swarms were observed. This suggests that the discovered phase relationships were independent of the stress condition of the volcano which was presumably changed by the eruption. The phase delay of 5 h does correlate with the maximum oceanic tidal loading. Mauk and Kienle thus suggest that the microearthquake activity lagging by 1 h is the result of direct triggering by tidal stresses and that the activity lagging by 5 h is related to the time of maximum oceanic tidal loading.

QUASARS

Nature of Redshifts

from a Correspondent

PLAGEMANN of Dunsink Observatory, Dublin, claims to prove (*Mon. Not. Roy. astr. Soc.*, **164**, 303; 1973) that the

quasars with compact radio sources and flat radio spectra are distributed anisotropically on the sky. If true this would be a significant result, casting doubt on the cosmological nature of the redshifts of these objects because if the microwave background radiation is, as most astronomers believe, cosmic black-body radiation left over from the fireball, then its extreme isotropy makes it improbable that the distribution of matter can show any very severe anisotropy on the large scale. Moreover, Plagemann's claimed anisotropy takes the form of a correlation with the Local Supercluster, a disk-like concentration of bright, nearby galaxies apparently centred on the Virgo cluster. This could only mean that these quasars are very nearby indeed, within about 30 Mpc.

It is perhaps surprising that the question of the true distances of the quasars has remained a matter of controversy

for so long. The trouble is that although some of the reported phenomena raising doubt have been laid to rest, others have turned up to keep the publications flowing. Little is heard now of Arp's pairs of radio sources on either side of peculiar galaxies, or of Burbidge's anomalous concentration of quasar redshifts around a value of 1.95. And three lines of work have pointed to at least some quasars with genuinely cosmological redshifts: the association of several quasars with small redshift with groups of galaxies with the same redshift, the inverse correlation of apparent radio size with redshift for the more extended quasars, and the existence of fuzziness round some small redshift quasars suggesting an underlying normal galaxy.

But like snakes from the head of the Medusa, new problems spring up to replace those already slain. The announcements last week in *Nature* by

Curious Behaviour of Carbon Fibres

FINE fibres of highly graphitised carbon have excited much interest because they are strong, stiff and light. The high strength and stiffness both stem from the strong c-c bonds in the graphite layer planes and, since the interlayer bonds are much weaker, the graphite lattice has of necessity a large anisotropy of both strength and stiffness. Accordingly, the mechanical properties of carbon fibre must vary with the degree of graphitisation of the lattice (a 'glassy' disordered arrangement of carbon atoms implies a comparatively weak 'average bond') and with the degree and nature of preferential alignment of the graphite layer planes where these are well developed. When, in addition, the quality and degree of alignment of graphite layers are also a function of position in the fibre cross section, the number of structural variables that affects mechanical properties becomes quite disconcerting.

Evidence has in fact accumulated that carbon fibres made according to the British process by pyrolysis of polyacrylonitrile have a duplex structure with a poorly graphitised core of low stiffness surrounded by a highly graphitised and aligned sheath of high stiffness. If, as seems likely, the sheath is of fixed thickness, then a reduction of the total fibre diameter will increase the proportion of sheath material and so raise the overall Young's modulus. Such dependence of modulus on diameter has been established, and the sheath/core hypothesis was advanced to explain this dependence.

In *Nature Physical Science* next Monday (December 3), Hart and Pritchard of Kingston Polytechnic confirm the

diameter dependence of modulus, and report on an attempt to test the sheath-and-core hypothesis more directly. Fibres originally pyrolysed at several different temperatures were submitted to attack by nitrogen dioxide at temperatures up to 925 K, using different pressures and periods of attack. Fibre diameters were reduced by as much as 80%. For fibres originally pyrolysed at 1,750° C, increases of modulus of up to 80% were established as the fibre diameter decreased; the amount of modulus increase depended on the conditions of attack, especially time and temperature. Fibres pyrolysed at 1,350° C showed negligible modulus changes in spite of thinning, and fibres pyrolysed at 2,750° C appeared resistant to attack.

The apparent paradox that removal of a stiff sheath leads to modulus increase is dealt with by the authors by the postulate that the attacking gas penetrates capillary pores in the sheath and preferentially attacks the poorly graphitised core. In the process, they believe that the sheath collapses onto the hollow core region and, in so doing, undergoes reformation of the graphite structure with the formation of new bonds. They believe that the inefficacy of low attack temperatures in increasing modulus is consistent with their postulate. It is not altogether clear whether the modulus increase is taken to be due to increased perfection of graphite structure, or increased alignment produced during the gas attack. The authors very properly conclude by pointing to the need for high-resolution electron microscopy to test their interesting ideas.

Wampler *et al.* (246, 203; 1973) of a pair of quasars a few seconds of arc apart but with very different redshifts, and by Hazard *et al.* (246, 205; 1973) of several examples of quasars apparently in clusters of galaxies but with much larger redshifts than the cluster could have, must raise doubts in the minds of all but the most diehard cosmological redshifters (by no means a rare species).

Not so long ago Karlsson (*Nature phys. Sci.*, 245, 68; 1973) was suggesting that the regular peaks in the distribution of quasar redshifts (Burbidge's 'periodicity') were absent from the quasars with extended radio sources, but present for the compact quasars. Unfortunately this was not established at a very significant level statistically.

This is again true for Plagemann's claim of anisotropy on the sky of compact quasars. When one works through his paper, past Fisher's method of statistical analysis of dispersion on a sphere, Monte Carlo computer algorithms, and topological considerations, it turns out that Plagemann's complete sample of compact quasars has only seven objects in it, and that the anisotropy disappears if three quasars at low galactic latitude have failed to be identified.

Clearly nobody is going to be moved from their favourite theory of quasar distances by that kind of statistics, or indeed by any kind of statistics. What is needed (as Wampler *et al.* point out) are good examples of associations of quasars and galaxies with different redshifts and signs of interaction. It is too much to hope to see a galaxy flare up, become a quasar, and change its redshift.

NUCLEAR STRUCTURE

New Giant Resonances

from our Nuclear Theory Correspondent

ONE of the most interesting events in recent years has been the discovery of new giant resonances in nuclei. The broad maxima in many reaction cross-sections around 20 MeV for light nuclei and at progressively smaller energies for heavier nuclei have long been known and are interpreted as E1 dipole resonances. They have been analysed microscopically as a coherent superposition of particle-hole excitations and more physically as the oscillation of the protons and neutrons in the nucleus against each other.

Enhanced cross sections have now been found at higher energies, and these are interpreted as giant multiple resonances of higher order. These resonances can be excited by inelastic-proton scattering, and a particularly striking example has recently been analysed by Geramb, Sprickman and

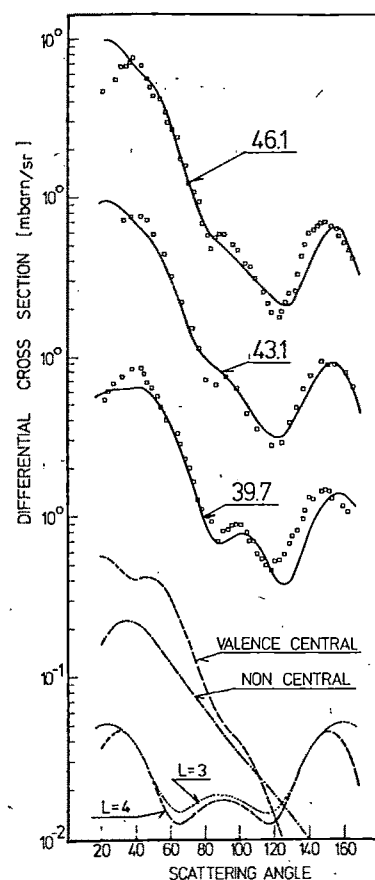
Strobel (*Nucl. Phys.*, A199, 545; 1973). They examined the differential cross sections for the $^{16}\text{O}(p,p')^{16}\text{O}$ reaction to the $J^\pi=2^-$ state at 8.88 MeV for proton energies from 23 to 46 MeV. Such cross sections are usually analysed by the microscopic distorted wave theory using an effective interaction consisting of central, spin and isospin-dependent and tensor components. Such a calculation gives a good account of the forward cross section but falls rapidly in the backward direction and completely fails to account for the prominent peaks found experimentally. This indicates that another mechanism is contributing to the reaction.

The forward peaks that are well understood by the direct distorted wave theory are inhibited in reactions involving a parity change compared with those involving no parity change. The backward peaks are thus more prominent in parity-change reactions, so these provide a better test of models devised to account for them. In the $^{16}\text{O}(p,p')^{16}\text{O}$ to the 2^- , 8.88 MeV state the conservation of angular momentum and parity require $S=1$ spin flip and parity change, implying a spin-dependent interaction or an exchange contribution.

The mechanism proposed is the excitation of a multipole giant resonance by the incident particle followed by decay of the resonance by proton emission. The nucleons remaining after emission combine with the proton initially responsible for exciting the resonance to give the final excited nuclear state. This process is called the core polarisation exchange mechanism. It is an exchange process because the emitted nucleon is not the same as the incident nucleon, as it is in direct processes. The direct core polarisation mechanism makes no contribution to the transitions involving a change of parity.

The cross section for this mechanism was calculated by the antisymmetrised distorted wave theory. The ground state of ^{16}O is a doubly closed shell, and the 2^- , 8.88 MeV state is represented by linear combination of particle-hole excitations. The incident and outgoing particles are represented by distorted waves generated by a complex optical model potential with spin-orbit coupling. The particle-core interaction is restricted to exchange contributions with isospins for the intermediate resonance states of $T=0$ or 1.

The data from 23 to 46 MeV were analysed assuming a direct contribution plus a core polarisation exchange contribution, and the amplitudes and energies of the giant resonance contributions were adjusted to optimise the fit to the inelastic scattering data. It was found that a good overall fit is obtained with giant quadrupole ($L=2$), octupole ($L=3$) and hexadecupole ($L=4$) resonances at 24, 35 and 42 MeV respec-



Differential cross sections for the $^{16}\text{O}(p,p')^{16}\text{O}^*(2^-, 8.88 \text{ MeV})$ reaction at 39.7, 43.1 and 46.1 MeV compared with distorted wave calculations including the $L=3$ and $L=4$ giant resonances. Also shown are the separate contributions of each reaction mechanism.

tively, in addition to the familiar dipole ($L=1$) resonance at 22 MeV.

The experimental differential cross sections for the $^{16}\text{O}(p,p')^{16}\text{O}(2^+, 8.88 \text{ MeV})$ reaction at 39.7, 43.1 and 46.1 MeV are compared with the calculations in the figure. Also in the figure are shown the contributions of the valence central and non-central interactions, which together account very well for the forward cross sections but not at all for the backward. In this energy range only the $L=3$ and $L=4$ giant resonances contribute appreciably, and as shown in the figure they are able to account very well for the backward peak in the experimental cross sections.

These higher order resonances have been found in several other reactions and in particular the $(p,2p)$ reaction seems to provide a promising way of exciting them. These resonances have widths of several MeV, so they are not so easy to study as narrower ones; it is therefore desirable that they should be excited in as many ways as possible to ensure that all the data are consistent with the interpretation. It is likely that such data will soon be forthcoming and will enable thorough studies to be made of these new modes of nuclear excitation.

Science in Australasia



Sydney Opera House [Australian Information Service]

In the following pages a few of those closely concerned review some of the science being done in Australia and New Zealand and look at the way in which the two countries support their scientists. There is one aspect of Australasian science, however, which deserves some comment but which can only be a matter of personal opinion.

In 1836 Charles Darwin wrote of New Zealand: "I believe we were all glad to leave; it is not a pleasant place and the greater part of the English there are the very refuse of Society"; and of Australia: "Farewell, you are a rising infant and doubtless some day will reign a great princess, but you are too great and ambitious for affection, yet not great enough for respect." Australasians have always been sensitive to the attention they receive from the rest of the world, particularly from the Europe-North America axis, and are keen to know whether they are now regarded with affection and respect and deemed to live in a pleasant place.

This concern has very realistic roots for scientists. Australasia is not a natural break in anyone's journey. It is not widely known either for unusually generous financial support of its scientists or for academic cloisters steeped in tradition. Journals arrive late, preprints are harder to come by and telephone calls to co-workers are not the casual affairs they can be elsewhere. There are thus reasons why scientists may not think seriously of ever visiting the area, let alone working there.

To this geographical isolation one has had to add a degree of self-cultivated philistinism amongst Australians. (Hereafter we speak of Australia rather than Australasia because of a more limited knowledge of New Zealand.) A. J. Marshall described their principal pastimes at the time of Darwin's visit as rum, horse racing and cricket, and it is a common belief beyond Australian shores that the same is still true. Australians are said to suffer from 'cultural cringe'—a desire to appear like sophisticated Europeans coupled with an obsessive fear of putting a foot wrong. The Australian image—and outsiders often tend to treat the country as a phenomenon rather than an equal—should not be underestimated as an inhibitor of a free flow of scientists every bit as powerful as the geographical

isolation. It is no accident that a majority of scientists live within reach of the cultural centres of the Northern Hemisphere.

All this is changing rapidly. Obviously the Sydney Opera House can be only a symbol, but by the same token the South Bank in London was also a symbol which has played a large part in the English cultural renaissance. Good news is heard on many fronts; there are new theatres and concert halls in Perth, Brisbane, Adelaide and Sydney. After many years in which Australian artists, writers and composers left their country to receive recognition, there now appears to be a reversal of the flow. The Australian Council for the Arts has been reorganised to allow professionals rather than rich dilettantes to run the show. It would be wrong to give Mr Whitlam's one-year-old government too much credit for all this; rather, the feeling in the country in favour of cultural change was also one in favour of political change.

If Australians are now making their country more appealing it is also the responsibility of outsiders to help break down the geographical isolation. The scientific community means little if communication between London, Boston and San Francisco is at the expense of that to Tokyo, Calcutta and Canberra. Science, even more than the post office and the airlines, needs more communal activity.

FUNDING AND CONTROL OF AUSTRALIAN SCIENCE	252
NEW ZEALAND'S NATIONAL RESEARCH ADVISORY COUNCIL AND THE USE OF SCIENTIFIC RESOURCES	255
SCIENTIFIC RESEARCH IN NEW ZEALAND	257
SCIENCE UNDER AN AUSTRALIAN LABOR GOVERNMENT	260
SEISMOLOGICAL AND GEOTHERMAL RESEARCH IN NEW ZEALAND	262
EARTH SCIENCES AND THE AUSTRALIAN CONTINENT	264
PEST MANAGEMENT IN AUSTRALIA	269
SOLAR POWER IN THE AUSTRALIAN ENERGY SCENE	271
ROCK ART IN AUSTRALIA	274
EMERGING PICTURE OF PLEISTOCENE AUSTRALIANS	278
PROSPECTS FOR ASTRONOMY IN AUSTRALASIA	282

Funding and Control of Australian Science

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Sir Rutherford Robertson discusses how the Australian science effort is organised and financed, and describes how the present government is approaching some of the problems.

AUSTRALIA, a federation of six independent states, each with its own parliament and civil service, as well as the federal parliament and civil service, has more complications in the administration and funding of science than many other countries. For example, since defence is a federal responsibility, all related scientific work is under the control of the Australian (also known as Commonwealth or Federal) government; by contrast, the states have substantial responsibilities for the administration of agriculture and fisheries and many scientists concerned with these activities are employed by the states, some of which have strong departments of agriculture. However, the federal government is the source of more than half the money which is spent on research and development. Analysis of the policies for research and development in Australia is further complicated at present because the Labor government which, under Prime Minister Whitlam, was elected in December 1972, has not completed plans for implementing its policies, some of which will have a considerable effect on science.

As in many countries in recent years, the increasing demands for research for community welfare, for health, for primary and secondary industry and so on, have resulted in constant discussion of the amounts that should be allocated both in total and for specific purposes. It was soon apparent that detailed knowledge is lacking of existing expenditures on science by the different agencies—federal, state, university, private institutions and industry—largely on account of the difficulty of dissecting amounts spent on science from total expenditure. The Department of Education and Science, established in 1967, planned to remedy this deficiency with a detailed study of the research and development expenditure in the fiscal year 1968–69 (Survey and Comparisons of Research Expenditures, known as Project SCORE)¹. The form of the survey is similar to, but not identical with, those conducted in other countries by the Organisation for Economic Cooperation and Development (OECD). This survey is not yet complete, but a private communication from the Department of Science provided the following information:

In 1968–69 the total expenditure on research and development by Australia was \$A342 million, of which \$A8 million was for work carried out overseas. Of the \$A334 million spent in Australia, 92% was incurred in the natural sciences and the remainder in the social sciences. Government plays a major role in both the funding and performance of research and development in Australia. Thus in 1968–69, the federal and state governments collectively contributed two-thirds of the funds, and research and development carried out in government agencies accounted for about half of the gross

expenditure. In contrast, the business enterprise sector contributed about one-quarter of the funds and accounted for about one-quarter of the expenditure on research and development² (see Fig. 1).

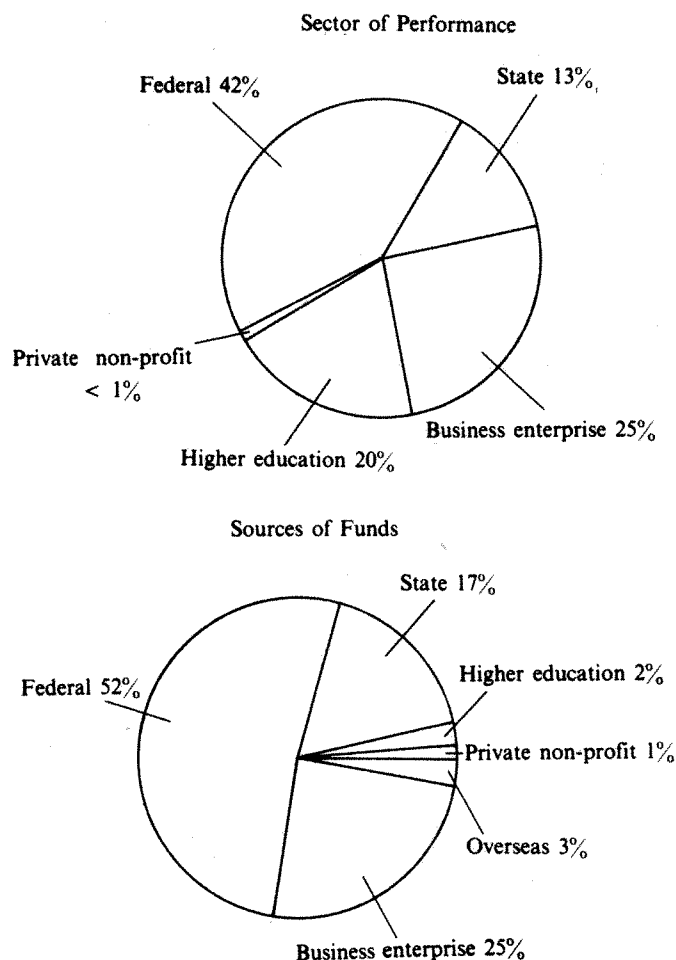


Fig. 1 Gross expenditure on research and development by sector of performance and source of funds.

The figures for 1968–69 expenditure on research and development in the university, state government and other non-profit sectors have not yet been published. The Department of Science advises that the university expenditure was \$A66 million (some from government grants) and state government expenditure was \$A42 million. The total expenditures are shown in Table 1.

Precise data are not available for Australia's present expenditure on research and development. An extrapolation based on the SCORE survey for 1968–69 indicates that current expenditure on research and development in the natural sciences, within Australia, lies between 1.0 and 1.1% of the gross national product, that is, between about \$A400 million and

Table 1 Expenditure on Research and Development* in Australia in 1968-69 (Irrespective of the Source of the Funds)

Sector of performance	Expenditure (\$A million)	Proportion (%)
Federal government	139	41.6
State governments	42	12.6
Higher education	66	19.8
Business enterprise	85	25.4
Private non-profit	2	0.6
Total	334	100

*In the natural and the social sciences

\$A1 = £0.62 = \$US1.49

\$A450 million per annum. Since 1968-69 there is reason to believe that private industry's share of the gross national expenditure on research and development has increased.

Government Science

The largest single group of scientists in Australia is the Commonwealth Scientific and Industrial Research Organisation (CSIRO), a statutory body responsible directly to the Minister for Science. In a total staff of about 6,000, over 2,000 are professional scientists, about half of whom have qualifications of PhD or higher. Research within the CSIRO is concerned with both primary and secondary industry, with standardisation of scientific apparatus and instruments (the National Standards Laboratory is part of the CSIRO), with collection and dissemination of scientific and technical information and with the publication of reports and periodicals. These research activities are organised into thirty-six divisions with some additional units and sections. Some divisions are directed to the needs of a particular industry; others are more specifically concerned with a single discipline. The budget of the CSIRO for 1972-73 was \$A77.7 million³. The approved estimates⁴ for 1973-74 are \$A93.6 million, of which \$A79.2 million will come directly from the Federal Treasury and \$A14.4 million will come from contributory funds which include such sources as the Wool Research Trust Fund, Meat Research Trust Account, Wheat Research Trust Account and so on, many of which are made up of compulsory contributions from the industries supplemented by government grants.

The CSIRO is administered by an executive consisting of five full-time and four part-time members. All the present members except one have scientific training and the present chairman is Dr J. R. Price, a well known organic chemist. The organisation has been a very successful body which, over the years, has established an environment for research that enables it to employ first class scientists who make a substantial contribution to solving national and industrial problems. The organisation is, however, constantly reviewing its responsibilities and its programmes. In releasing the 1972-73 report, the chairman spoke of the way in which, during the past year, the CSIRO has broadened its traditional research goals to take account of rapidly changing community needs, a development which calls for closer collaboration with social science, mainly with the social scientists in the universities. When tabling the report in parliament, the Minister for Science expressed his intention "to see that the research work carried out by the CSIRO continues to be 'people oriented'".

The next largest group of scientists is concerned with defence research. Of the money spent on research and development by the federal government in 1968-69, approximately \$A57 million¹ was spent in this way, most being spread over four major defence research establishments of the Department of Supply, namely, the Weapons Research Establishment (principally guided weapons and applied physics, including electronics; Woomera test range for joint

Australian-British interests); Defence Standards Laboratories (principally research into defence materials; operates Joint Tropical Research Unit in conjunction with British authorities); Aeronautical Research Laboratories (principally aeronautics); and Central Studies Establishment (operational research).

Approximately 6,500 man-years of effort were devoted to this programme in 1968-69, of which about 20% was carried out by professionally qualified scientists or engineers. Broad policy for defence research and development is in the hands of the Chief Defence Scientist. Advice to the minister is provided by the Defence Research and Development Policy Committee, chaired by the Chief Defence Scientist, and by the Defence Science Board, chaired by the Secretary, Department of Defence.

The Atomic Energy Commission, which was established in 1953, has wide responsibilities including, in addition to research, advice to the government on uranium exploration and use, construction and operation of generating plant, and making grants-in-aid to research. The commission spent \$A13.8 million in 1972-73 and has approved estimates of \$A14.9 million in 1973-74 (ref. 4). The total staff is approximately 1,130, of whom 300 are professional scientists operating in eight divisions. Active cooperation with universities is achieved through the Australian Institute of Nuclear Science and Engineering, of which each university is a member. The Atomic Energy Commission is a statutory body, reporting to the Minister for Minerals and Energy, and governed by a commission of five, two full-time and three part-time.

Other federal government bodies concerned with science include the Post Office, the Bureau of Mineral Resources of the Department of Minerals and Energy, the Bureau of Meteorology and the Antarctic Research Division of the Department of Science, and the Commonwealth Serum Laboratories, National Biological Standards Laboratory and Australian Radiation Laboratory of the Ministry of Health.

Departments concerned with science in the different states mainly carry out research and development for the agricultural and pastoral industries, for fisheries and for forestry but, in recent years, substantial contributions have been made by departments engaged in research and development support for secondary industry and other activities.

Science in Universities

The Australian Universities Commission advises the Australian government on the financial assistance for the maintenance and development of the Australian universities in each triennium. Up to the present, the support has come from both federal and state governments. Thus in the current (1973-75) triennium, 46% of the total income came from the federal government, 35% from the states, 11% from fees and 10% from miscellaneous sources, including endowments⁵. The Australian government has announced its intention to abolish all fees from 1974 so dependence on federal government funds will increase. Funds earmarked for university research (about half those estimated as spent on research in universities) are from four main sources: (a) general recurrent funds recommended by the commission, about 22.2% in 1970; (b) special grants for research recommended by the commission, about 11.6%; (c) grants from other government sources, particularly the Australian Research Grants Committee and the National Health and Medical Research Council, about 44.9% from federal and 2.1% from state grants; (d) other grants, contracts and donations from private sources, about 19.3%. As might be expected, most of the research funds (35.5%) were devoted to science faculties, 19.0% to medical faculties, 14.4% to engineering, 12.9% to agriculture and 3.4% to veterinary

science—a total of 85.2% to the natural science-based faculties. The remaining funds came mainly from general university grants which are financed mostly by government.

The Australian Research Grants Committee, established in 1965, has consistently “sought to direct itself to supporting the most outstanding and promising research being carried out in Universities and research institutions”⁶. The committee invites submissions from individuals or teams and bases its selection on reports from referees and assessors.

The funds distributed by this committee, not confined to science, amounted to 19.6% of the funds earmarked for research in universities in 1970 (ref. 5). Approximately 13% of the Research Grants Committee allocations went to the humanities and social sciences, another 13% to the engineering and applied sciences and the remaining 74% to the physical, chemical, biological and earth sciences.

Medical research in universities is partly supported by the National Health and Medical Research Council which distributes grants for research on the advice of its subcommittee, the Medical Research Advisory Committee. In 1968–69, the year of the SCORE survey, it distributed \$A1.6 million, two thirds of which was for university research.

Research in Industry

Of the \$A198 million spent on research and development by the federal government in 1968–69, \$A9 million or 5% went to the business enterprise sector (private communication from the Department of Science). In 1967, the federal government established the Industrial Research and Development Grants Scheme, which is administered by a board that now reports to the Minister for Secondary Industry. In the first four years of its existence, the board distributed \$A44 million to firms which had, themselves, spent about \$A200 million⁷ in the same period on increased research and development mostly within the companies, though some was spent on contract research. Companies supported in this way cover a wide range as regards both size and products (such diverse things as building materials, food and electrical equipment). Of the 500 or so companies so far assisted, nearly half had previously carried out no research; moreover the professional level of the employed research personnel has risen markedly overall since the scheme started. These developments have, in some measure, countered the criticism, often heard a few years ago, that Australian firms were dependent on overseas industrial research ‘know-how’. The smaller firms in Australia often regarded themselves as unable to support a research department and some of the larger firms, subsidiaries of still larger overseas companies, drew on the research expertise of the parent company in Britain, Europe or the United States. Some international companies which started research departments in Australia have closed them in periods of economic recession, giving rise to some alarm about the possibility of not having adequate industrial research teams in this country; the activities of the Industrial Research and Development Grants Board are important in ensuring that industrial research is increased and maintained.

Independent Research Institutions

There are a few independent research institutions in Australia, the most famous of which is the Walter and Eliza Hall Institute of Medical Research; other well known institutions are the Australian Mineral Development Laboratories and UNISEARCH, the contract research company sponsored

by the University of New South Wales. There are no research bodies with sufficient endowments to provide the full funding for the institution and most draw heavily on federal and state granting bodies. Several private foundations such as the Potter Foundation, the Myer Foundation, and the Ramaciotti Foundation for medical research, also support scientific work with grants. The museums, at least one in each state, are supported primarily by state government money.

Policy for Science

During the past decade there has been an increasing demand for a science policy machinery in Australia; the problems have been reviewed in an important article by Peres⁸, to be published shortly. The present government, while in opposition, had recognised, in 1965, a need for a comprehensive national approach to science. In 1968, the Science and Industry Forum of the Australian Academy of Science⁹ recommended the establishment of an independent Advisory Committee on Science and Technology. After some delay the Liberal government, then in power, established such a committee which held its first meeting in October, 1972; it was disbanded not long after the present government came into power in December 1972. The Minister for Science has stated that he intends to set up a Science Council with advisory powers, and an announcement is expected soon.

Meanwhile the minister (W. L. Morrison) announced to the media on October 21 that he had asked the OECD to carry out a wide ranging examination, early next year, of Australia's scientific and technological activities. It is suggested that the way in which Australia uses science should be analysed and a coordinated plan developed. The two or three member panel appointed by the OECD will visit Australia in March or April next. This is part of the government's plan to see more of the efforts of Australian scientists and technologists being turned, in future, to social and environmental problems. The results of such a survey and the policy which the government intends to adopt, particularly in relation to review and control of scientific expenditure, will be awaited with great interest.

I thank the officers of the Australian Government Department of Science for their assistance in providing the data referred to in this article.

¹ Department of Education and Science, *Project SCORE: Survey and Comparisons of Research Expenditure. Report 1. Research and Development Expenditure by the Commonwealth Government 1968–69* (Australian Government Publishing Service, Canberra, 1972).

² Department of Trade and Industry, *Survey of Industry Research and Development Expenditure in Australia 1968–69* (Australian Government Publishing Service, Canberra, 1972).

³ Commonwealth Scientific and Industrial Research Organization, *CSIRO Twenty-fourth Annual Report 1972–73* (CSIRO, Melbourne, 1973).

⁴ Parliament of the Commonwealth of Australia, *Estimates of Receipts and Summary of Estimated Expenditure for the year ending June 30, 1974* (Parliamentary Paper, Canberra, 1973).

⁵ Australian Universities Commission, *Fifth Annual Report* (Australian Government Publishing Service, Canberra, 1972).

⁶ Australian Research Grants Committee, *Report 1970–72* (Australian Government Publishing Service, 1972).

⁷ Australian Industrial Research and Development Grants Board, *Fifth Annual Report 1971–72* (Australian Government Publishing Service, Canberra, 1972).

⁸ Peres, L., *Science and Technology in Public Policy in Australia* (edit. by Forward, R.) (Cheshire, Melbourne, in the press).

⁹ Science and Industry Forum, Australian Academy of Science, *Science Policy Machinery for Australia* (Australian Academy of Science, Canberra, 1968).

New Zealand's National Research Advisory Council and the Use of Scientific Resources

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The role of New Zealand's 10-year-old National Research Advisory Council has been chiefly to advise the Minister of Science on the research activities of government agencies with particular reference to the total expenditure and priorities for expansion in various fields of application of science. In this article its chairman reviews the functions of the council and its achievements, and outlines future developments. Particular importance is attached to closer integration of the research carried out by government agencies, the universities, research associations and industry.

SUCCESSFUL application of scientific and technological knowledge to New Zealand's problems requires, as in other countries, not only human, financial and material resources, but an institutional framework providing the mechanism for coordinating national policy-making. In New Zealand, decisions on national scientific policies are made by the Minister of Science and the Cabinet, subject to the guidance and control of parliament during annual consideration of the Estimates. Scientific research programmes are planned and carried out in the various research divisions of government departments, in the universities and in the research associations and other scientific institutions. Advising the government on a coordinated national policy for scientific research which takes into consideration the work of all these agencies is the role of the National Research Advisory Council (NRAC).

Council's Form and Functions

The NRAC is directly responsible to the government through the Minister of Science. Its comprehensive functions, as defined in the Act which set it up in 1963, are to advise the minister on the promotion, development, planning and coordination of scientific research and services in New Zealand. In most countries today, governmental science policies are concerned with all scientific and technological activities, ranging from basic research to the practical application of new knowledge. The 1971 United Nations World Plan of Action for the Application of Science and Technology to Development emphasised the need for national science policy-makers to be responsible for all matters where science and government meet. The NRAC's terms of reference are wide enough to allow it to fulfil such a role.

The council consists of nine members. One of six who are appointed by the Governor-General on the recommendation of the Minister of Science is appointed chairman. The other three are the permanent heads of the Ministry of Agriculture and Fisheries, the Department of Scientific and Industrial

Research, and the Treasury. The present appointed members include four company directors, a university professor and a farm manager.

Members of the council broadly represent the scientific and technological community in New Zealand, but they cannot be expected to have the expertise or time needed to investigate every problem that comes before them. The council is therefore assisted by three standing advisory committees covering primary production, manufacturing and processing, and research related to the natural and social environment. Members of the council act as chairmen of these committees.

The council is an advisory body only. Its role is not to centralise and administer national scientific effort, but rather to coordinate and continuously to evaluate its effectiveness. The Act requires the council to determine priorities among the research activities of the various government departments, having regard to research done by other organisations such as the universities and the research associations. It also plans and coordinates the government's association with industry in the promotion of research, and its help in shaping the government's attitudes towards the promotion and maintenance of research associations is important. It also recommends the awarding of scholarships and fellowships to facilitate the training of government research workers, and can promote cooperation in scientific matters with governments and organisations in other countries as well as with international organisations.

Science Budget

A comprehensive Science Budget, prepared annually to assist the council in advising government on appropriate allocation of resources to various areas of scientific activity, enables all government science activities and science grants to be dealt with in the context of one forward programme. Each department's work is classified according to a dozen major activity headings, rather than by scientific disciplines. These groupings are agriculture, forestry, fisheries, minerals, manufacturing, building and construction, transport, the natural environment, the social sciences, human health, fundamental research, and what is termed other scientific services. These major activity groups are subdivided into thirty-seven categories, in which the council ascertains what work is under way, the resources devoted to it and the relevant cost. It also obtains forecasts of resources and costs needed to maintain existing levels of effort in each group over a forward-planning period of 3 years. It analyses new work and any extension of existing work that is proposed, and the benefits predicted to accrue from it. From this background information, the council recommends to the government what it considers desirable growth rates in scientific manpower for each activity, with an estimate of the likely cost. Priorities in allocation of manpower are a prime consideration in recommendations, because manpower is the most common and constant factor in scientific planning and expenditure.

The government then decides on an appropriate growth rate—it is 5 per cent overall for 1973–74 and is expected to remain the same next year—and within this approved frame,

work the details of each department's research efforts are agreed on.

Science Budget allocations for the 1973-74 financial year (excluding supplementary estimates still to be announced at time of writing) are shown in Tables 1 and 2.

Table 1 Science Budget Allocation 1973-74 by Activities

Activity	Direct departmental allocation* \$ thousand	Grant allocation* \$ thousand	Total allocation* \$ thousand
Agriculture	14,934	2,097	17,021
Forestry	3,380	39	3,419
Fisheries	1,379	28	1,407
Minerals	1,066	124	1,190
Manufacturing	2,087	172	2,259
Building and construction	856	214	1,070
Transport	722	51	773
Natural environment	8,634	244	8,878
Social sciences	435	256	691
Human health	625	14	639
Fundamental research	5	707	712
Other scientific services	812	44	856
Public buildings	2,200	—	2,200
Total	37,125	3,990	41,115

*\$NZ1=£0.62=\$US1.49

The council's role is at all times advisory; formulation and implementation of research programmes are the prerogative of departments; government funds for science are voted by parliament to the departments and not to the council. The council ensures that overall priorities are observed and that government receives a good return for its substantial investment in science. The council observes the way the science programme is being implemented by visits to research divisions and stations, primarily by its three advisory committees. It relates its overall recommendations to national plans and targets through its function as a sector council of the National Development Council.

University Research

Medical research is the province of the Medical Research Council, but the NRAC is concerned with the place of the universities in New Zealand research. The six universities receive most of their finance from the government as block grants at five-yearly intervals. Part of these grants, \$700,000 in 1973, is allocated by the University Grants Committee (UGC)

Table 2 Science Budget Allocation 1973-74 by Departments

Department	Direct departmental allocation* \$ thousand	Grant allocation* \$ thousand	Total allocation* \$ thousand
Agriculture and Fisheries	9,844	613	10,457
Defence	841	5	846
Education	61	915	976
Electricity	5	8	13
Forest Service	2,832	36	2,868
Internal Affairs	306	—	306
Justice	42	2	44
Labour	177	4	181
Lands and Survey	—	12	12
Maori and Island Affairs	—	10	10
Scientific and Industrial Research	15,235	2,195	17,430
Social Welfare	109	10	119
State Services Commission	61	—	61
Transport	3,687	23	3,710
Works	1,725	157	1,882
Public Buildings	2,200	—	2,200
Total	37,125	3,990	41,115

*\$NZ1=£0.62=\$US1.49

to research. This allocation shows as part of the Science Budget in expenditure by the Department of Education, but there is also considerable provision for research by staff and students in the balance of the block grant paid by the UGC to the universities to meet running costs. The Science Budget provision also includes annual grants to certain universities to support research institutions established with the cooperation of the government, such as the Agricultural Engineering Institute and the Tussock Grasslands and Mountain Lands Institute at Lincoln College, and the Poultry Research Centre at Massey University. Increasing use is being made of the universities through the letting of government research contracts, principally through the Department of Scientific and Industrial Research, which will spend an estimated \$61,000 on contracts in 1973-74.

Industrial Research and Development

The other major source of government funding of research is the Industrial Research and Development Grants Scheme, established in 1969 and administered by the Department of Trade and Industry. This provides for grants and subsidies to corporations and persons who have undertaken industrial research and development in New Zealand for the benefit of New Zealand. Government grants for industrial research and development projects under this scheme in the year ended March 31, 1973 totalled \$1.16 million.

Highlights of Past Year

Improved auditing capacity by the council of research work in government institutions has resulted from the establishment of the three advisory committees to focus the attention of experts in various fields on a continuous review of research priorities.

A comprehensive review of the most appropriate type of government funding of the ten research associations, based on an evaluation of their effectiveness and appropriate rates of growth, is well advanced. There may be a need for a different sort of funding from the traditional dollar-for-dollar subsidies. Some restructuring of associations could also be timely to encourage them to work more closely together where there is a need for a multidisciplinary approach to research problems.

Another form of assistance to industry being investigated is industrial and production technology. Research which could bring widespread benefit could include the use of mini-computers for process and production control. The council is investigating the needs of the textile industry as a pilot project with a view to establishing a methodology which might be applicable in other sectors of industry.

The country's present productive capacity is in no small measure due to its excellent agricultural research institutions. The council has been reviewing the work of several government research stations to assess the balance of research effort between them. Two areas of concern have called for closer examination. The council is investigating the approach to solving the pasture pest problems which are so adversely affecting many of New Zealand's farming areas, and has recently reported on proposals to reorganize and expand fisheries research within the Ministry of Agriculture and Fisheries. One of its committees is also giving priority to the need to coordinate freshwater research, in which many agencies are working on similar problems.

The council is also reviewing the need for overall organization in social science research, and has discussed with the University Grants Committee ways of encouraging research relevant to the national interest. The council considers there is need to strike a balance between the universities continuing to encourage fundamental research and the concern of the government to ensure that sufficient attention is given to post-graduate training in fields of national importance. The legiti-

mate requirements of academic freedom and the national interest can probably only be met satisfactorily if substantial government funds are provided through more than one channel. One such channel should naturally continue to be direct to the university system and the other through government departments by way of long-term grants, fellowships and short-term research contracts. Such a system would reconcile the autonomy of the universities with the legitimate interests of government in the national welfare. It would also serve to improve understanding and communication between university and government scientists to their reciprocal advantage.

Council's Future

New Zealand's research resources are limited. We must ensure that all are used to the full, and that the research is relevant to our needs. It is essential in a small country like ours to concentrate on those areas we know best and where we have a special contribution to make, drawing on the resources

of larger countries for basic research in areas outside our competence and limited resources. The danger at present is a tendency to spread our research efforts too broadly and to investigate related aspects of the same problems without sufficient planning. A closer relationship between the research efforts of the government, the universities, technical institutions and industry is vital to make our research more truly national and product-orientated. We shall also probably need to expand the system of intergovernmental agreements of the type announced in September between the United States and New Zealand, to facilitate cooperation and the exchange of information and scientific expertise. In determining future government research priorities, we shall need to pay more regard to research done by other organizations. I believe the NRAC will move away from concentrating on details of government departmental research into the broader field of determining an overall policy that will be needed if New Zealand is to meet its economic and social objectives more effectively and realistically.

Scientific Research in New Zealand

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In this article an attempt is made, with particular emphasis on university experience, to give an overall view of scientific research in New Zealand and its special features as seen through the eyes of a research worker.

In this article I describe scientific research in New Zealand and compare it, where possible, with the practices in the United States and Britain. In order to give an overall picture of scientific research in New Zealand I will first describe the funding and organisation of research within the university system and within the Department of Scientific and Industrial Research (DSIR). An attempt will then be made to sketch the broader features of scientific research within the universities.

New Zealand Universities

There are seven autonomous university institutions¹ in New Zealand, all funded by the central government through the University Grants Committee (UGC) on a quinquennial basis. They had a total of 35,000 students enrolled in 1972. In contrast to the situation which exists in the United States, academic staff in New Zealand universities are paid on the basis of a twelve-month year. This means that full academic salaries are met from the quinquennial grant. In addition technicians' salaries and day-to-day running expenses are also met from this source. The maintenance and running expenses of buildings housing both teaching and research are also a charge on the quinquennial grant. Their actual construction costs are funded separately, but still, through the UGC. Research equipment

can sometimes be bought from 'setting up' grants made available when a new building is occupied, providing its use in teaching can be justified. Other research costs are funded from several sources, the chief ones being:

- (i) Research Grants Committee of the UGC. The awards² made by this committee in 1971 were NZ\$612,000* and its budget for 1973 is NZ\$700,000. Most of this money is used to purchase research equipment.
- (ii) Research committees of the individual universities. The budget of the Research Committee of the University of Auckland for 1973 is NZ\$50,000. (This university, the largest in New Zealand, has 9,500 students of whom 1,050 are enrolled for doctoral or masters degrees.) At present this committee seeks to satisfy the research needs of individuals who need rather small grants for minor pieces of equipment, microfilm, books, travel and field expenses and the like.
- (iii) Medical Research Council³. In 1972 expenditure by this body was NZ\$1.87 million.
- (iv) The Medical and Scientific Research Committees of the National Lottery Board⁴ each disbursed NZ\$125,000 in 1971.

The concept of funding a major facility (for example, an accelerator or reactor) and assuming its running costs for the first few years is unknown in New Zealand. Instead, research grants are made to individuals for a specific research project. This contrasts vividly with the way in which nuclear physics research, for instance, is funded in universities in the United States by the National Science Foundation (NSF), where grants are generally made to a 'principal investigator' who is the director of a major facility (for example a tandem accelerator). Any suggestion that such a system should operate

*The present exchange rates are £1.00=NZ\$1.61; NZ\$1.00=US\$1.49

in New Zealand would probably be severely criticised especially by the sub-professorial staff in the universities. The advantage of funding the individual directly is that it is relatively easy for a research project in a new field to be started, especially one which does not demand a large investment at the beginning. The major drawback is that research activities in many departments become very fragmented: the independence of the academic is no myth and with few constraints each staff member tends to go his own way.

Because of the small size of the scientific community in New Zealand, the allocation of research money is undertaken by the various research committees. This is very different from the method adopted by the NSF, where all grant proposals are refereed by at least one peer scientist. When it comes to judging the real worth of most research proposals, the committee members would probably feel that they were acting as informed laymen rather than as experts in the subject. That the system works as well as it does is a considerable tribute to the abilities of the people who make up the various research committees. It has, however, been pointed out that it is often difficult for such a committee to separate the significant from the trivial research.

DSIR Support for Research

The DSIR is an example of a government department engaged in research. Its expenditure in 1971 (ref. 5) was NZ\$12.1 million, whereas in 1970 it was NZ\$10.4 million. (The comparable figure⁶ for university research, including all MRC funded research was NZ\$4.3 million in 1970.) The DSIR accounts for approximately 44% of government expenditure on science. Research in agriculture and the environment accounted for NZ\$7.5 million of its 1971 expenditure. Very properly, there is a heavy commitment to applied research and development, and the individual scientist will generally have less freedom than his counterpart in the universities to choose his own research projects. Requests for funding are channelled through the normal administrative pyramid where relative priorities are established at several different levels. (This, however, is as it would appear to a man wishing to initiate some particular research project. Probably a more general procedure is that the director of a research institute will call for proposed expenditures for the next year from his section leaders and the proposals assembled by him will move up from there.)

(In the universities by contrast, priorities are established only at the very top—by the UGC Research Grants Committee.) Normally before a major piece of equipment (more than NZ\$5,000) can be bought, it must be in the year's budget. Even then it is still subject to Treasury approval. A further complication is that money not spent in one financial year cannot be carried over into the next. To overcome this problem, however, an 'advance order' may be made against next year's expected capital equipment budget if, for instance, delivery time is expected to be long. In an emergency, of course, money budgeted for 'consumables' may be used to finance what would normally be a 'capital equipment' item, a procedure which is not uncommon in most countries.

Research in the Universities

What conditions are necessary to encourage the successful prosecution of scientific research in New Zealand? As in all countries the first prerequisite is adequate funding. In addition, because of New Zealand's remoteness and small size, additional criteria need to be satisfied. Turning to the first point, the latest available comparative figures⁷ are for 1967. In that year expenditure *per capita* by New Zealand on domestic research and development was approximately one-third of the expenditure by the USA and two-fifths of that by Britain and Canada

(In a study by the Organisation for Economic Cooperation and Development on reviews of national science policy, the following comparisons are made for 1967 of gross domestic research and development expenditure for economic and social purposes (in US \$ per head of population): United States \$34.5; Britain \$24.0; Canada \$23.7. For New Zealand the comparable figure⁷ was \$10.00) My impression is, however, that since 1967, the relative position of New Zealand has improved somewhat. It is obvious too that the demand for research support within the university system far exceeds the supply; in 1971 the research committee of the UGC received 287 applications for grants totalling NZ\$2.9 million. They were only able to make awards totalling NZ\$0.6 million to 122 applicants². The positions of some departments are perhaps not quite as bad as these figures would indicate. Setting up grants received by a department upon occupying a new building have often been a great help in obtaining necessary research equipment, providing its use in the teaching programme (including graduate teaching) is justifiable. Almost every avenue of scientific endeavour now needs adequate computer facilities. Until very recently these were woefully inadequate in almost all New Zealand universities. With the installation, at a cost of approximately NZ\$3 million, of five Burroughs 6700 computers within the universities, the situation has now improved a good deal. Remote terminals, however, are all but unknown and the computers are still short of memory and peripheral equipment; computer facilities in New Zealand universities are still rather modest when compared with those available in comparable universities in the USA or Britain. In many cases technical staffing of science departments appears to be adequate when compared with overseas laboratories. Although academic staff have almost always spent time in overseas laboratories, technical staff rarely have. For this reason it is sometimes rather hard to develop in New Zealand the technical competence in certain specialised areas which can be taken for granted in laboratories in the USA or Britain. Many skills at the technical level are best transferred by direct contact at that level. Finally there is much variation in the standard of accommodation for both people and equipment. Those who are housed in new buildings are obviously better off than those in old or interim accommodation.

Small size

Returning now to the problems peculiar to New Zealand, perhaps the most noticeable feature is that the small size of the scientific community means that it is difficult, or impossible, to obtain the stimulation which seems so vital for worth-while research to take place. The most serious problem is generally the lack of critical listeners with an interest common to your own, whether it be research or teaching. This was stated somewhat differently by a colleague: "there is no recognition of your work within New Zealand". This deficiency, however, is exacerbated by artificial constraints which isolate the staff in the different universities from one another. (The Research Grants Committee through their policies of funding the individual contribute further to this isolation. My colleague's comment also reflects the fact that, quite sensibly, the development of the same research interests at different universities has not been encouraged.)

For instance, in three years as Professor of Nuclear Physics at Auckland I have not been asked to give a seminar or colloquium in any university in New Zealand other than my own (although I have given a short course at the Institute of Nuclear Sciences). In my time in the USA, however, I was invited to speak at Berkeley, Stanford, Yale, University of Pennsylvania and Brookhaven National Laboratory. The chief reason for this lack of interaction between the different universities would appear to be the difficulty of obtaining money to pay the travel costs of seminar speakers. Within even a major department there is no such thing as a seminar fund and each time you wish

to invite a speaker, a special application must be made. It is a hardy seminar organiser who persists for very long under such a régime. In addition, although cooperation between government laboratories and the universities is generally good, there is at least one area where such collaboration has been frowned upon in the past by the government department concerned. We certainly cannot afford the luxury of this sort of insularity in such a small country. Another artificial constraint is the virtual impossibility of obtaining support to go to overseas conferences (especially in the Northern Hemisphere). Even when money is forthcoming, the idea of full payment of expenses is quite foreign and almost without exception the individual concerned will need to dig quite deeply into his own pocket. In addition, provisions for conference travel within Australasia are inadequate; at Auckland the Department of Physics, with a permanent academic staff of 24, has been allocated NZ\$1,000 for next year for such purposes. Until this year it has been virtually impossible to obtain such support for PhD students. The situation now is not much improved.

Sabbatical leave provisions for New Zealand academics seem to be somewhat more generous than are those of their counterparts in most universities in Britain and the United States. This statement, however, is certainly not true of scientists employed in government laboratories. Although they find that provisions for travel within New Zealand are adequate, like their university counterparts, money to attend overseas conferences is extremely difficult to get. There is no doubt that a vigorous policy of secondment to, and staff exchanges with, laboratories overseas would greatly benefit scientific research in New Zealand. (The cost need not be great.) Sabbatical leave is, in general, available to all staff members at senior lecturer or higher (equivalent in the USA to Associate Professor or higher). It generally consists of one year of leave (after six years of service) on full salary plus fares for the individual.

Delays and Advantages

An important feature of any good research laboratory is its holding of scientific journals and books. With some exceptions these are reasonable. Time of arrival, however, is also important. Typically *Physical Review* is between two and three months late. There is a similar problem with conference proceedings and books ordered from the Northern Hemisphere. Some may argue that this is not important. The inability to read the journals until three months after one's colleagues in the Northern Hemisphere, however, is not conducive to a stimulating research environment. An obvious solution, if economically feasible, is to airfreight at least the important journals and conference proceedings.

Delays occur when ordering equipment. Most equipment purchases must be made through a centralised purchasing section of the Education Department in Wellington, the capital city. I am told that there are advantages in this, but its only apparent effect is to increase the time taken to obtain equipment by about two months. A solution to this problem would be for each university to have its own purchasing department. An additional characteristic which stems directly from New Zealand's small size and isolation is the difficulty of initiating new research quickly if it involves the purchase of a new type of equipment. For example, you may decide that a certain type of spectrometer would probably be the best tool to solve your problem. In the United States or Britain a telephone call to two or three manufacturers would probably result in an offer to demonstrate the instruments within a few days. You could then make a judgement of the worth of the equipment by using it yourself. At 12,000 miles this is not often possible and probably even with one's own limited knowledge you know more about it than anyone else in New Zealand; there is not even anyone to talk to. The other side of this coin is that, in a small laboratory,

it is often relatively easy to assemble quickly a number of people with the required skills to undertake a particular project. If no major new equipment is required such an undertaking can often be concluded more quickly than in a larger institution.

Some scientists, however, are at an advantage working in New Zealand. In most laboratory-based research, a worker is in direct competition with his colleagues in the generally better equipped laboratories overseas. On the other hand, there are quite a large number of research areas where the researcher in New Zealand, because of New Zealand's geographical position (even its remoteness!) or some other special feature, can find that he is in a better position than a researcher in a more advanced country. Examples that spring to mind are oceanography (New Zealand is in the middle of the water hemisphere), geothermal energy investigations and a number of areas in agricultural research. The smaller size of research establishments in New Zealand also means that a scientist is forced to be less of a specialist and to master a wider variety of skills than in large laboratories.

Shortage of Fellows

Finally, perhaps the biggest deficiency of all is the paucity of post-doctoral fellows. In every good university or national laboratory I have ever had anything to do with in the United States or Britain, the post-doctoral fellows (and the similarly situated non-tenured assistant professors in North America) have played a very large part in the research activities. The reasons are not hard to find: they are young, they can devote a large fraction of their time to research and work harder at it than many established researchers. They are often thoroughly conversant with their subject. With an academic staff of about 500, there are six post-doctoral fellows at the University of Auckland (these figures exclude the medical school). The situation is not much different at the other universities. The contrast between the funding of equipment purchases which in some areas is seen to be adequate and the demands for post-doctoral fellows is that the latter must compete with all the other demands put on a university's block grant, whereas the funds available to the research committee of the UGC have been earmarked for that purpose. (They are² "... sequestered from the gross amounts calculated for the total block grant and are intended to be used principally for large purchases of equipment. . . .")

Many of the above points would apply equally well to scientific research in government laboratories in New Zealand. I would be surprised if they had no relevance to the Australian scene. Perhaps it should be said finally that the conditions under which scientific research is carried out in New Zealand have improved a great deal in the past few years. I think they will continue to improve in the near future. If it is felt that I have been unduly critical then my plea is that until we identify deficiencies in the system, we cannot overcome them. Furthermore, there is no point in undertaking scientific research in New Zealand unless you can do it at least as well as it can be done elsewhere.

¹ *Reports of the University Grants Committee for 1972*, App. E3 to the Journals of the House of Representatives of New Zealand (JHR) (1973).

² *Report of the Research Committee* (University Grants Committee; 1971).

³ *Report of the Medical Research Council of New Zealand*, App. E11 (JHR) (1973).

⁴ *Report of the Lottery Board of Control*, App. H22B (JHR) (1972).

⁵ *Report of Department of Scientific and Industrial Research*, App. H34 (JHR) (1972).

⁶ *New Zealand Year Book* (Department of Statistics, Wellington, 1972).

⁷ *ibid.* (1970).

Science Under an Australian Labor Government

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IN the course of a special interview during the preparation of this article, Mr William Morrison, the first Australian Minister for Science, said that there are absolutely no votes in science in this country. For scientists in Australia, looking for a greater public and political involvement in their work, this realistic assessment brings small comfort. For the Labor government, twelve months in office this week (after twenty-three years in the wilderness of opposition), it is unfortunate that the largely constructive and uncontroversial record of the minister and his new Department of Science has had no effect on the fortunes of the Labor Party.

At the time of the last report in *Nature* on the politics of Australian science¹, as demonstrated at the Australian and New Zealand Association for the Advancement of Science (ANZAAS) Congress, the Whitlam government was carrying all before it. But in the three months since then there has been a rapid and marked fall in the degree of popular support for the Labor party and its policies. The previously dominating profile on the domestic scene of Mr Gough Whitlam and his government has been eroded by the loss of a crucial by-election, by the political effects of rapid inflation, by a series of mishandled announcements of major decisions, and by the rejection in the spring session of Parliament of a number of important measures by a hostile Senate where the government is in a minority. An early honeymoon for Labor in the press has now changed, even among enthusiastically radical journalists, to a critical and sceptical mood about the style and substance of Labor in power.

All this is germane to any assessment of the present state and future prospects of science in Australia. A minor Cabinet reshuffle last month left Mr Morrison still holding his two portfolios of External Territories and Science. Self-government for Papua New Guinea, the second major stage in the territory's move towards full independence, is due to be implemented on December 1. Then, Mr Morrison's major preoccupation will ease and he could be expected to have more time for the Science portfolio.

Such expectations are, however, qualified by speculation that a further Cabinet reshuffle predicted for early in 1974 could include a promotion for Mr Morrison out of a relatively low ranking ministry.

Labor has had a policy for science and technology written formally into its manifesto for some time; the latest amendments list thirty-three points of policy, mostly couched in general terms. The preamble talks of integrating science policy with social and economic policy in achieving national goals. Point 3 of the Platform on Science and Technology specifies "a minister with direct responsibility for science and technology". But on assuming office in December 1972, Mr Whitlam only established a Ministry for Science; technology was left out and was not included by name in any other ministry.

Under the preceding Liberal and Country Party coalition government, the administration of science had been tagged on to the big vote-getter and budgets of education. In the formal hierarchy of ministries which then obtained (under Labor, all twenty-seven ministers are equal in formal status and salary, even the Ministers for Sport and Foreign Affairs), the Ministry for Education and Science was a powerful political springboard. Indeed, the first Minister for both Education and Science, the then Senator John Gorton, went on to become Prime Minister, albeit for a short time. Gorton and his several



Fig. 1 Mr William Morrison (left), Minister for Science, and Dr J. R. Price, Chairman of the CSIRO.

successors were at pains to deny that a national policy for science was possible; but apart from setting up a project to collect data on the financing of research in Australia, they never tried seriously to test that proposition. Yet, the principal achievements of Australian science and its broad directions were settled under the oversight and funding, if not the declared direction, of the Liberal-Country Party régime; with few exceptions, these have been accepted as a proper inheritance by the Labor Party.

The CSIRO (Commonwealth Scientific and Industrial Research Organisation) grew under the previous government to its present eminence in size and reputation, both locally and internationally. The CSIRO budget for 1972-73 (the Australian financial year runs from July to June) was \$A68.6 million, of which \$A56.1 million came from the Treasury and the remainder from various industries, predominantly rural, for supportive research.

The Liberal-Country Party coalition instituted some order and growth into the funding of research outside CSIRO with several grant schemes; these were started in the 1960s, and without exception have been continued by the Labor government. The ARGC (Australian Research Grants Committee) disburses funds to individuals and small teams in universities, predominantly but not exclusively, in science. The NHMRC (National Health and Medical Research Council) gives money for clinical research and medically oriented biology. The IRDG (Industrial Research and Development Grants) comprise money for research and development activity within commercial industry. The full picture is difficult to unravel, though, because a number of government departments

have sizeable research budgets, each university has its own funds for allocation on departmental bases, some universities benefit from industrial support and general benefactions, and there is a fair amount of silent support for medical research from drug companies. Within the Department of Science, project SCORE (Survey and Comparison of Research Expenditure) is gathering basic data on these points.

Some idea of the level of support can be gained from the triennial budget for 1973-75 of the ARGC; this amounts to \$A20 million and four areas have been specifically earmarked—\$A0.9 million is allocated for new initiatives in upper atmosphere science; \$A0.9 million for new initiatives in marine science; \$A0.65 million for multidisciplinary research and \$A0.55 million for a major 'national facility' in NMR spectrometry. Four weeks ago the first, eagerly awaited annual list of detailed grants awarded under the Labor government were announced; the total figure of \$A6.5 million was only a very modest \$A0.7 million larger than the last grant under the previous government. The NHMRC has \$A13.5 million to disburse in the same triennium.

The mood of researchers in Australia has changed over the past decade from one of skimp-and-scrape, often of despair with a consequent wastage of talent to overseas, to moderate satisfaction with the degree of support. Research funds are spread fairly widely (there are a thousand recipients of the latest ARGC funds); Australian egalitarianism peeps through, to the detriment, however, of some world-standard projects in astronomy which demand major capital grants to get off the ground. The odd political fact was that the Liberal-Country Party politicians could never articulate their achievements in this field. The lack of specialised science correspondents in the media did not help, and this situation is hardly different now. As Mr Morrison said, there are no votes in science in Australia. Yet there was, and is, much to show off. At least Mr Morrison's publicity efforts, coupled with the establishment of a separate Department of Science, have given the organisation of science in Australia a more cohesive identity than previously.

The spectacular instruments of the Australian astronomers have been highly productive of important discoveries—radio-astronomers using the big dish at Parkes gained fame by their studies of quasars, their colleagues at the Molonglo (or 'Mills') Cross through work on pulsars, those at the Narrabri Stellar Interferometer for classical measurements of the sizes of stars, and those at the Culgoora radioheliograph for their moving pictures of the radio sun. Australia won its first two Nobel Prizes for medical research (interestingly, before significant government funding started) through the virologist and immunologist Sir Macfarlane Burnet and the physiologist Sir John Eccles (they were joined as fellow laureates this year by the novelist Patrick White). The development of analysis by atomic absorption spectroscopy in Melbourne and the remarkable Self-twist Spinning Machine of the Geelong laboratories are two multimillion dollar export earners from original CSIRO work.

Under the Labor government, the Minister for Science has gained control of some of the scientific activities which were previously dispersed under various other Ministers, but even now does not have government-sponsored research to himself, any more than did his Liberal-Country Party predecessors. The Education Department looks after universities, Health has the NHMRC scheme, Minerals and Energy has the Bureau of Mineral Resources and the Atomic Energy Commission (now sadly moribund as regards its principal purpose, nuclear power, which has been postponed indefinitely by the government), Supply covers defence research and Secondary Industry has the IRDG. These inheritances have been joined by two new departments interested in scientific and social research, Environment and Conservation, and Urban and Regional Development. Prominent among the ministerial staffs of these creations (including Science) have been members of the small but previously vocal Social Responsibility in Science

Societies, which have fallen remarkably silent under Labor rule.

Orientation towards social needs and multidisciplinary approaches are the special stamps Mr Morrison wants to place on Australian science ('people science' is the ungrammatical slogan coined by his staff). With this in mind he first looked critically at the CSIRO. Dr J. R. Price, Chairman of the 6,600-strong organisation, reflected on the changed mood in the CSIRO's twenty-fifth annual report, released to Parliament last month. He contended that it is unfortunate and incorrect to use the terms 'people oriented' and 'industry oriented' in such a way as to suggest they are irreconcilable. Research which benefits 'industry', he wrote, also benefits 'people'—and conversely. A case cited is the process for polyunsaturated meat and dairy products², patented by the CSIRO, which was licensed to a company controlled from overseas before the Labor Party came to power and imposed restrictions on licensing to foreign companies. The CSIRO has, however, reflected the political and social climate through regrouping and redirecting some of its existing divisions and creating new ones. For instance, the new Divisions of Land Resource Management and Land Use Research have been grouped with the older Division of Soils; together they will provide basic information (ecological, hydrographic, geographic and so on) for planning the development of Australia's coastal fringe, where the majority of Australia's 13 million people are being crowded, in an uncoordinated fashion, into what may become the world's longest conurbation. These and other moves, like the employment of a few social scientists, seem now to have smoothed over a somewhat sticky relationship between the CSIRO and the Minister for Science in the first frenetic months of Labor rule. In the August budget, the CSIRO won its first significant expansion in professional staff for some years.

The immediate future of Australian science will be dominated by four main growth areas. First, astronomy will be boosted by the commissioning throughout 1974 of the sophisticated 3.9 m (154 inch) Anglo-Australian optical telescope. Second, marine science is being encouraged by the imminent establishment of the Australian Institute of Marine Science as well as several other projects. Third, medical research will be broadly based, but will continue to develop centres of excellence in physiology and immunology. Fourth, solar energy research, a field in which the CSIRO devices for low grade heating probably lead the world, will be supported politically and popularly; the CSIRO is establishing a special small unit to study the whole, broad question.

Among the unique initiatives of the Labor Minister of Science has been a popular move into the definition and enforcement of consumer standards on sound scientific grounds; a special commission, headed by a physicist, has been set up for the purpose. A Biological Resources Council has recently been established to make an inventory and collection of the country's flora and fauna, which, considering their uniqueness and diversity, are remarkably unknown. And the Organisation for Economic Cooperation and Development (OECD) has been invited to investigate Australian science.

To assist in the development of a policy for science and technology, the previous government established, rather late in the piece, an Advisory Committee on Science and Technology; this was quickly axed by Mr Morrison soon after taking office, with the stated intention of implementing the fourth plank of the Labor Party platform, namely the establishment of a Science Council. This has, however, proved more difficult than was thought at the time of winding up the previous ACST. Until the minister can push through Cabinet and Parliament the necessary legislation to set up this Science Council and give it independent powers, a national policy for science in Australia is likely to remain largely *ad hoc* and in a political backwater.

¹ *Nature*, 244, 534 (1973).

² *Nature*, 245, 10 (1973).

Seismological and Geothermal Research in New Zealand

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In both solid Earth and atmospheric sciences New Zealand has international responsibilities stretching from the equator to the south pole and from 165° E to 155° W, representing almost 6% of the Earth's surface.

WITHIN the New Zealand region are many interesting geological and geophysical manifestations. New Zealand itself consists of a currently active plate margin superimposed on an upper Palaeozoic-lower Mesozoic geosyncline, though this over-simplified view ignores many aspects of New Zealand's geology. It does, however, define fairly well the areas with which the work of most of the country's Earth scientists has been concerned. The Pacific-Indian plate margin is readily identified as continuing to the Kermadecs and Tonga to the north and, in the other direction, to the triple junction south of Macquarie Island. The New Zealand Geosyncline is disposed in a complex series of sinuous curves from New Caledonia perhaps to the Chatham Islands. From the large variety of work being done in this region by Earth scientists we shall discuss two topics. In one, seismicity, New Zealanders have often held views at variance with workers in other regions. In the other field, that of geothermal energy, development has been led by New Zealand for the past two decades.

Seismicity

The most obvious effect of the plate margin on the community at large is the risk to life and property from earthquakes and volcanism. A magnitude 7 earthquake shook Wellington in 1848, only eight years after the founding of the settlement, and was followed in 1855 by an even closer earthquake, now presumed to be of magnitude 8. It was from a study of this earthquake that Sir Charles Lyell made one of the earliest associations of contemporaneous fault breakage accompanying a major earthquake. The first Milne seismographs were installed at Wellington in 1900 and at Christchurch a year later. From these have grown the present network consisting of twenty-six stations in the main islands and eight in outlying territories extending from Samoa to the Antarctic. New Zealand's geophysical involvement in the Pacific stems from the First World War, when the established Observatory at Apia in Western Samoa passed from German to New Zealand administration. There are now five New Zealand-controlled seismograph stations in the Pacific to the north of New Zealand, covering one of the most active seismic areas of the Earth. To the south, stations at Campbell Island and Scott Base are in completely different geophysical environments. The two main strengths of the New Zealand seismograph network are its extent and its unified control. All records from the network are finally analysed at the Seismological Observatory in Wellington. This enables the earthquakes of the whole region to be examined together, and the interrelationship of seismicity and other geophysical features to be evaluated.

Northern Seismic Region

A unique characteristic of northern New Zealand is that its principal geophysical phenomena (gravity anomalies and man-

tle earthquakes) pass through the continental region and thus the seismological network virtually straddles an island arc.

The most striking feature of the seismicity is the lack of correlation of shallow earthquakes with the visible geology. Whereas the deep and intermediate earthquakes form a well defined zone dipping to the west beneath the North Island and the north of the South Island, the shallow earthquakes display a 'pepper-pot' effect of wide scatter (Fig. 1). That this effect is not a result of imprecise location has been recently demonstrated by detailed micro-earthquake surveys along the Alpine and other major fault systems, carried out by New Zealand and American parties. These surveys confirm the locations given by the standard analysis of the New Zealand Seismological Observatory. The reason for this paradox seems to lie in the depth of the earthquakes. Those earthquakes that are located in the top few kilometres can often be associated with a fault trace, but much of the activity appears to be in the lower crust, and related more to underlying mantle activity than to superficial geology. Indeed there seems to be a change in earthquake mechanism from dominantly compressional for earthquakes less than 20 km deep to dominantly tensional for deeper earthquakes.

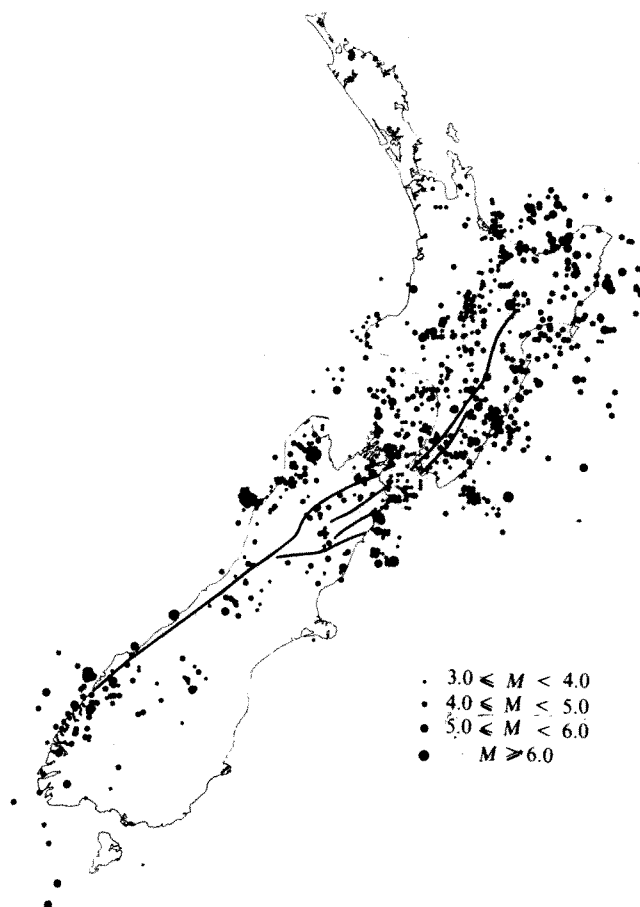


Fig. 1 Upper crustal earthquakes, 1955-66. Improvement in the seismograph network since 1966 has shown that the southwestern part of New Zealand (Fiordland) is, seismically, the most active part. Only the principal faults are shown. Numerous smaller fault zones exist, particularly in the eastern half of the North Island. —, Major active faults

Alpine Fault

Like New Zealand, California also consists of a current plate margin superimposed on an older geosyncline. The many similar features of the San Andreas and Alpine Faults have often invited comparison which has, at times, become identity. But historical statistics and short-term micro-earthquake studies have both failed to identify the Alpine Fault as similar to the San Andreas Fault in the seismological sense. Earthquakes and micro-earthquakes in the central part of the South Island are not aligned along the Alpine Fault though they seem to be confined to the upper part of the crust. Composite focal mechanisms from the diffuse activity in the region obtained by a Lamont-Cornell group¹ show that a regional NW-SE compression dominates the tectonics, this direction being nearly normal to the Alpine Fault. The resulting conclusions that the Alpine Fault is now undergoing a large component of thrust faulting with consequent uplift of the Alps and that the greater part of the transcurrency pre-dated the current orogeny are consistent with much geological opinion in New Zealand. They are in disagreement with the views of some plate tectonists who wish to have the whole 500 km shift take place after mid-Miocene.

Fiordland

The visible Alpine Fault ends at Milford Sound, one of New Zealand's most scenic localities (and its wettest). At this northernmost of the fiords intermediate depth earthquakes recommence (Fig. 2) but continue southwards for only 150 km. Shallow earthquakes persist into the Macquarie Ridge and hence to the triple junction south of Macquarie Island. Where the deeper earthquakes begin to peter out a gravity anomaly pair begins, the positive anomaly over Fiordland revealing a mantle at little more than 5 km depth and the gravity low offshore indicating probably 30 km of low density material below a sea which is 4,000 m deep. As the gravity anomalies diminish to the south the geophysical picture (Fig. 2) is dominated by the magnetic anomaly of the north Macquarie Ridge. The interpretation of the transition of the Alpine Fault to the Macquarie Ridge in terms of the complex and abrupt geophysical changes has so far defied anybody's tectonic intuition. The geological maps of Fiordland show virtually no active faulting in this, the most seismic region in New Zealand, though whether this is due to the difficulties of exploration in this rugged country is a moot point.

There is a real danger in considering that, in New Zealand, the zones of greatest earthquakes are necessarily concentrated along surface expressions of faults, or in accepting that studies of physical processes accompanying or preceding Californian earthquakes will be relevant to the understanding of destructive seismicity in New Zealand. It is true that there are many spectacular faults in New Zealand and that some of these have moved during large earthquakes, but detailed plots of epicentres show little relation to the lineations of active faults. It is from an awareness of their own environment that New Zealand seismologists have not always accepted without question the faulting mechanism of earthquake generation. From the same awareness, the general optimism overseas about the prediction of earthquakes is not unequivocally shared. However a telemetered seismic network, an order in scale down from the main network, will be established in the Wellington region during the next two years to test current theories in New Zealand conditions.

Geothermal Energy

Though generally a hazard, the plate margin makes a positive contribution to human welfare by providing heat. The thermal waters of New Zealand have been used for many years in spas, bathing pools and for house heating, but it is only twenty-five

years since the Government made the decision to attempt to use geothermal energy as a source of electric power. One field was developed quickly and the New Zealand Electricity Department's station at Wairakei, which now has an output of 150 MW, began producing power in November 1958. About the same time the large mill of the Tasman Pulp and Paper Company was sited so that steam from the Kawerau field could be utilized in the integrated energy complex of that concern. Since then development of geothermal fields has been negligible, perhaps as a result of the discovery of a large gas field (Matii) off the west coast of the North Island.

The early development of Wairakei was mainly due to engineering initiative spurred on by the United Kingdom Atomic Energy Authority's temporary interest in the production of heavy water; for the scientists were still feeling their way in matters of geothermal exploration. Since those early years,

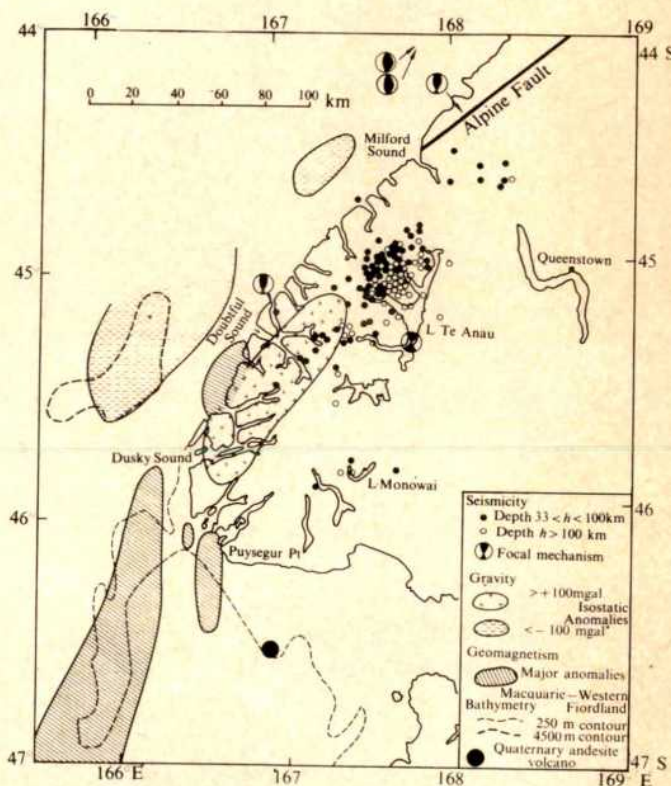


Fig. 2 Composite geophysical map of Fiordland. Subcrustal earthquakes only are shown, for the years 1966-68, 1971 and 1972. Focal mechanisms of some shallow earthquakes reproduced from Scholz *et al.*¹.

however, an enormous amount of systematic geological, geochemical and geophysical work has laid the basis for a proper appraisal of total resources and of each individual field.

Although most fields are indicated by some form of surface thermal activity, the size of the reservoir is best explored by electrical resistivity methods, for the thermal waters contain about 1,000 to 2,000 p.p.m. Cl. Figure 3 shows the fields so far delineated by electrical techniques, and it is conservatively estimated that at least 1,000 MW of power is available from these areas, the ultimate amount probably depending on permeability conditions within the fields. Although the whole gamut of electrical techniques has been tested during the past decade, including dipole-dipole and transient E-M, the simple traverse with a Schlumberger spread is still the most convenient and effective method of defining the fields.

A major problem in exploration remains—the very difficult (impossible?) one of predicting permeability or fissure availability at depth from surface measurements. Although the size

of a heat source can be defined quite well by geophysical methods, the crucial problem of prediction of draw-off rates is dependent almost entirely on geological inference, until tested by expensive drilling. Since some areas are covered by fairly recent ash showers or lacustrine deposits, even knowledge of geology can only be derived by stratigraphic drilling, and

extrapolation and interpolation of the chaotic volcanic and sedimentary rock units are fraught with difficulty; recently an attempt has been made to detect concentrations of fissures by resistivity anisotropy. Conservative estimates of power available can be made considering the system as a static reservoir. True reserves are, however, dependent on the recharge of the system; detailed, regularly repeated gravity surveys combined with levelling are being used at Wairakei to supplement well data in an effort to understand the dynamic characteristics of the reservoir.

As usual, the devotion of a large scale scientific effort to an economic objective has induced a number of intensive offshoot studies. The nature of hydrothermal alteration in rocks was the first of these, followed by the experimental geochemistry of the interactions between rock and hot-water. Perhaps the latest is the examination of currently forming base-metal and gold-silver mineralization in the Broadlands field and its relationship to mineral deposits in similar, older and now inactive environments elsewhere. The Taupo Volcanic Zone has a rapidly increasing population based mainly on timber "farming". The burgeoning problems of siting all the accoutrements of civilisation (like houses, schools, roads and cables) in thermal regions have resulted in traditional, *ad hoc* individual temperature surveys being replaced by an airborne emissive infrared survey of the major towns and their environs.

On a larger scale, the major fields seem to occur as fairly regular, vertical, hot water pipes along or just behind the volcanic front. The nature of the heat source and the mechanism of heat transfer (to the almost wholly meteoric waters) continue to preoccupy the mathematical physicists, and the geophysicists are seeking deeper sounding methods of high enough resolution to contribute to the source problem. Meanwhile the acquisition of skills in the exploration for and exploitation of this once esoteric form of energy has resulted in a great demand from other countries for New Zealand consultants—a demand which, if not carefully watched, may stultify or inhibit geothermal research and development within New Zealand.

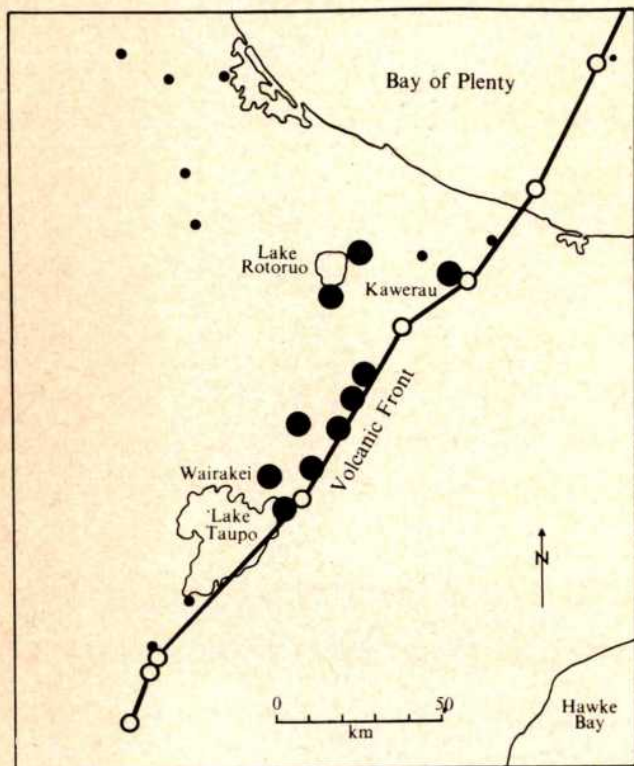


Fig. 3 Locations of geothermal fields. The volcanic front has been drawn by joining the easternmost volcanoes (○). ●, Fields where substantial areas of ground resistivity $< 20 \Omega$ are known to occur (normal ground resistivity is 200 to 500 Ω). •, Other, relatively unsurveyed, areas with hot springs.

¹Scholz, C. H., Rynn, J. M. W., Weed, R. W. and Frohlich, C., *Geol. Soc. Am. Bull.*, **84**, 3297 (1973).

Earth Sciences and the Australian Continent

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Dr McElhinny discusses some recent activities and an important new development.

SPECTACULAR developments have taken place in the Earth sciences in recent years, and ideas about the structure and evolution of the Earth have changed profoundly. Because of the importance to Australia of its mineral resources, not least among the consequences of these developments has been their effect on the interpretation and knowledge of the geology of the continent and its margins. The simplified map of the surface geology in Fig. 1 shows that the western portion of the

Precambrian shield is bordered to the south by the Late Precambrian to Cambrian Adelaide geosyncline and to the east by the Palaeozoic Tasman Orogenic Zone. With the advent of plate tectonics it was at once realised that the presence of a number of serpentine belts in the Tasman Orogenic Zone could be diagnostic of the past locations of island arc complexes and consuming plate margins (Fig. 1). Ultrabasic and basic rocks in intimate association with serpentinites are suggestive of the former presence of ophiolites representing oceanic crust and mantle material, and in plate tectonic theory ophiolite emplacement occurs at consuming plate margins. It is not surprising therefore that there has been a resurgence of interest in regional geology and much rethinking of many aspects of Australian geology in terms of plate tectonic theory.

On May 31 and June 1 of this year the Queensland Division of the Geological Society of Australia held an important

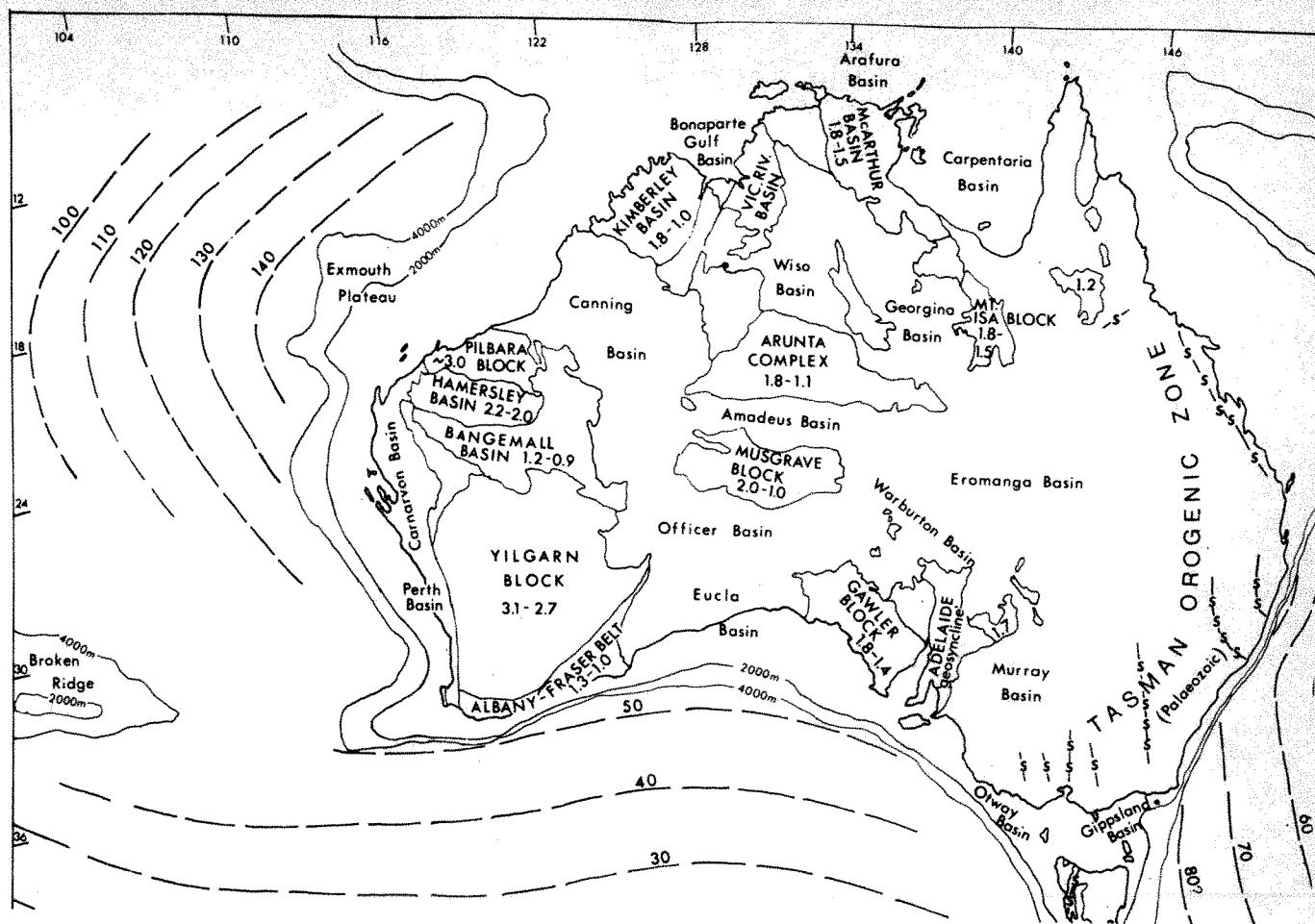


Fig. 1 Simplified surface geological map of Australia and the surrounding ocean floor. Precambrian regions are outlined with names in capitals and ages in units of 10^9 yr. Serpentine belts (S) are indicated in the Tasman Orogenic Zone. Isochrons showing the ages of the surrounding ocean floor are given in units of 10^6 yr.

symposium in Brisbane on the subject of the Tasman Orogenic Zone in honour of Professor Dorothy Hill, who retired as professor of geology in the University of Queensland. The serpentinite belts in the Tasman Orogenic Zone tend to become progressively younger eastwards and it has been supposed that a series of island arc and intra-arc basins merged with the main Australian assemblage during the Palaeozoic¹⁻³. Although some of these early attempts at applying plate tectonic models to the evolution of the zone met with some criticism, they have nevertheless led to a renewal of interest in the synthesis of the wide spectrum of geological data (stratigraphic, petrological, geochemical, structural and geophysical) available for this zone. New field programmes have then been designed to test the hypothesis in great detail. There seems little doubt that the concepts of plate tectonic theory offer the most credible basis for understanding of the evolution of the zone.

Geochronological studies largely undertaken at the Australian National University in conjunction with the Bureau of Mineral Resources have established the basic age patterns of the major Precambrian cratons^{4,5} (Fig. 1). The spectacular mineral discoveries of the sixties in Western Australia have led to much detailed work being carried out in the Precambrian shield. On May 23-26, 1970 the Western Australian Division of the Geological Society of Australia held a symposium on Archaean rocks in Perth and this was attended by over five hundred scientists from Australia and overseas. The proceedings have been published as Special Publication No. 3 of the Geological Society of Australia (December 1971). There is a general feeling that the nature of geological activity has changed during geological time. The major structures have

have formed parts of a global tectonic arrangement. Thus of special interest is the problem of whether or not the concepts of plate tectonics can be extended back to the earliest Precambrian⁶. Palaeomagnetic data from the various cratons in Africa already show that relative movement between them must have been very small over the past 2,200 m.y.⁷, in spite of the existence of younger intervening orogenic belts of several ages. The first results from an extensive palaeomagnetic programme through the Australian Precambrian tentatively show this to be true also for Australia. It is, however, interesting to note that studies of some Western Australian Archaean greenstone belts have led to the suggestion that the development of the first primitive continental crust, now represented by these greenstone belts, was produced directly from a basaltic crust by the same process as continental crust is produced from oceanic crust in present day island arcs—by means of seafloor spreading and plate tectonics⁸. Do these belts therefore represent relics of the oldest island arcs? A more provocative suggestion has been made as a result of the extensive studies of lunar material undertaken at the Australian National University. (The group of four Principal Investigators—A. E. Ringwood, W. Compston and S. R. Taylor at the Australian National University and J. F. Lovering at the University of Melbourne—together received more of the Apollo Moon samples than any other group outside the United States.) Perhaps the Archaean greenstone belts are the terrestrial equivalents of lunar maria⁹. It has been suggested that the production of lunar maria basins was accompanied by similar impacts on the Earth. The Archaean greenstone belts are interpreted as very large impact scars

composition and thereafter evolving with further magmatism, deformation and metamorphism to the present Archaean greenstone belts. Whether or not this hypothesis stands the test of time, it represents an object lesson for the critics of basic scientific research. Who would have thought that the studies by Australian scientists of lunar samples collected by United States astronauts could possibly have had any bearing on the origin of some of Australia's mineral-bearing terrains?

Precambrian stratigraphy in Australia has in the past relied on geochronological studies, which in turn have depended upon the availability of igneous rocks for dating. Some of the early work on the Rb-Sr dating of shales was undertaken in the Australian Precambrian, but the problem remains as to how one interprets isochrons drawn through the data points in terms of an age of deposition. After an initial burst of activity in this field, little has been done during the past 5 years and the uncertainties remain to be resolved. In the Soviet Union over the past decade stromatolites have become a standard tool for the subdivision and correlation of Late Precambrian sedimentary rocks and new methods and classifications have been developed. While this work was still in its infancy Professor M. F. Glaessner at the University of Adelaide brought it to the attention of the Western world^{10,11} and initiated research in this field in Australia. This work has now demonstrated the world-wide applicability of the Russian stromatolite assemblage zones¹². It is particularly appropriate that the Australian stromatolite distribution has been used to test the generality of the Soviet scheme because important pioneering work on the origin and stratigraphic distribution of stromatolites was carried out in Australia early this century. The first major treatise on stromatolites and the biostratigraphy of the Australian Precambrian and Cambrian¹³ marks a milestone in palaeontology because as yet no other detailed biostratigraphic studies in this field have been published outside the Soviet Union.

Offshore Exploration

The first offshore exploration of Australia was carried out in 1954 when the Bureau of Mineral Resources recorded an aeromagnetic survey of the Gippsland Basin. By 1964 most of the likely areas were taken up in petroleum concessions. It is only subsequent to first oil explorations that the age of the ocean floor around Australia has been determined. Between Australia and Antarctica¹⁴ and in the Tasman Sea¹⁵ ages have been found from analyses of marine magnetic anomalies in terms of the seafloor spreading hypothesis (Fig. 1). This resulted from work at the Lamont-Doherty Geological Observatory in conjunction with the Marine Geophysics Research Laboratory at the University of New South Wales. Off Western Australia the age of the ocean floor has been determined by the basement sediment isochrons plotted from results of leg 27 of the Deep Sea Drilling Project¹⁶ (Fig. 1). Legs 21, 22 and 26 to 30 inclusive of the Deep Sea Drilling Project (JOIDES) have involved exploration of the oceans around Australia and three Australian scientists have acted as Co-Chief Investigators on the Glomar Challenger (C. C. Von der Broch, leg 22; J. J. Veevers, leg 27; G. H. Packham, leg 30). Six other scientists from the Bureau of Mineral Resources and various universities have also participated in these cruises. The Bureau of Mineral Resources has just completed a geophysical survey (contracted) of the continental margins, but there is an urgent need for further work in physical oceanography and marine geology and geophysics. Australian scientists, especially those in universities, have had to rely on ships of other countries (notably the United States) or else on limited assistance from Australian naval ships. Australia has more than 12,000 miles of coastline and fronts on three oceans, but there is as yet no permanent fully equipped oceanographic ship. The need is urgent and fundamental, for without one or more ships there is little prospect of further development of

Extensive investigations of the offshore regions have been carried out during the past decade by oil exploration companies. Government subsidies for these investigations, although soon to be discontinued, were extremely liberal but in return the exploration companies were required to submit well completion and other exploration subsidy reports to the Bureau of Mineral Resources. Such an enlightened policy has resulted in a much freer flow of information from the oil companies than in other parts of the world. The community of Earth scientists in Australia has benefited greatly from this arrangement. As a result the *Australian Petroleum Exploration Association (APEA) Journal* has blossomed into an important source publication particularly for summaries of work carried out in the offshore regions. It is at once apparent from syntheses of this work that oil geologists have very soon come to the realisation that the evolution of continental margins can be related to the new global tectonics¹⁷. Especially important is the discovery that the initial rifting between Australia and Antarctica preceded by 100 m.y. the formation of the mid-ocean ridge that resulted in the final separation of Australia and Antarctica about 50 m.y. ago. Igneous rocks of similar age to the mid-Jurassic dolerites of Tasmania and Victoria Land, Antarctica have now been found at various sites in the Otway Basin and on Kangaroo Island. These date the formation of the Otway Rift Valley between Australia and Antarctica into which was deposited Upper Jurassic and later sediments now found off the south coast of Australia^{18, 19}. The relationship of Australian continental margin oil and gas discoveries to stages in the development of continental margins and the evolution of ocean basins as portrayed by an oil geologist¹⁷ is shown in Fig. 2.

Geophysical Measurements

In January 1973 the Second International Conference on Geophysics of the Earth and Oceans was held in Sydney under the auspices of the Australian Institute of Physics, the Australian Institute of Mining and Metallurgy and the Australian Society of Exploration Geophysicists. This was as successful as its predecessor, also held in Sydney (in January 1971), and showed there has been a heightening of interest and much activity in exploration geophysics in Australia over the past few years. The gross geophysical features of continental Australia are best viewed from gravity, seismic and other measurements. The new Bouguer anomaly map of Australia issued by the Bureau of Mineral Resources is the result of

CONTINENTAL MARGIN STAGE	PERTH BASIN	WESTERN N.W. SHELF	GIPPSLAND	OCEAN STAGE	OCEANIC EVENT
Prograding	Tertiary	Tertiary	Holocene	Mature	Termination of spreading
	Upper	Upper	Pleistocene		Sea floor spreading
	Cretaceous	Cretaceous	Pliocene		
			Miocene		
Readjustment	Lower Cretaceous	Lower Cretaceous	Oligocene	Young	Block faulting and thinning of crust
		☆	Eocene		
	Jurassic	Jurassic	Palaeocene		
	Triassic	☆	Cretaceous		
Initial Stage	Permian	Triassic		Initial	Uplift
	Upper Carboniferous	Permian	Jurassic		

●, Oil; ☆, Gas

Fig. 2 Relationship of Australian continental margin oil and gas discoveries to stages in the development of continental margins



Fig. 3 Summary of certain geophysical information relating to the crust and upper mantle beneath Australia. •, Seismic epicentre $m \geq 4.5$.

measurements at over 500,000 stations; 10 mgal contours are shown derived from a minimum density of one station per 130 km², representing a better coverage than has been achieved on any other continent. Ninety per cent of the continent is now covered at this minimum density, the final 10% will be completed in 1974. The gravity map shows some interesting features including a series of alternating negative and positive anomalies in Central Australia with maximum-minimum differences of 100 to 150 mgal. Two of these negative anomalies (Fig. 3) correspond with the Amadeus and Ngalia sedimentary basins, but they are too large to be explained by the sediments alone. It seems that some feature in the deep crust or upper mantle contributes to these anomalies.

Australia is a quiet continent seismically, with only Antarctica having less contemporary activity. A few earthquakes of magnitude $m \geq 5.5$ occur each year, the largest recorded being of magnitude 7 near Meckering, Western Australia, on October 14, 1968. Earthquake epicentres^{20,21} follow three main trends (Fig. 3) and it has been suggested²¹ that these trends divide the continent into four subplates, although this is very speculative at this stage. Seismic studies of the crust and upper mantle in Australia have been reviewed by Dooley²² and Cleary²³. The discussion here will be restricted to the eight large scale refraction experiments carried out during the past seventeen years. In the first of these use was made of the nuclear test explosions at Maralinga in 1956 and in the last use was made of two large chemical explosions in 1970 and 1971 detonated during quarrying operations at the Ord River Dam site in northern Australia. The last two explosions each produced seismic amplitudes equivalent to about a magnitude 4.5 earthquake and were the first in Australia to produce reliable data beyond 1,000 km (ref. 24). P_n velocities obtained from these experiments are shown in

Fig. 3. They are higher beneath the shield and appear to increase systematically from east to west. P_1 velocities derived from these experiments are also significantly higher in the Precambrian shield region than in eastern Australia. There is good evidence for an intermediate layer in all parts of Australia, with an average depth of about 20 km to the Conrad discontinuity²³. The crustal thickness averages about 40 km, the variations in thickness being apparently unrelated to topography. Studies of P wave station anomalies²⁵ show that stations in south-east Australia have large positive residuals, whereas those to the west have negative residuals. These trends have been confirmed from observations of the Cannikin explosion in the Aleutian Islands on November 6, 1971 using a set of temporary seismic stations across 1,700 km in the southern part of Australia²⁶. The trend towards more negative anomalies appeared to be most pronounced over about 500 km near the centre of the traverse, a region that includes the eastern boundary of Precambrian rocks (Fig. 3). The results imply a strongly developed low velocity layer in the upper mantle in eastern Australia which disappears as the Precambrian shield boundary is approached.

Variations in heat flow in Australia show a similar trend to the seismic variations with very high values observed in eastern Australia and very low values in the Western Australian shield²⁷ (Fig. 3). Two studies of electrical conductivity structure of the crust and upper mantle from magnetic variation studies using arrays of twenty-five magnetometers have been made across south-central Australia in 1970 (ref. 28), and in south-east Australia in 1971 (ref. 29). The principle of mapping higher temperatures in the crust and upper mantle through the related higher electrical conductivity is of prime interest in these geomagnetic deep soundings. The results of these

shows a long curved conductor in the lower crust or upper mantle running north-south close to the Flinders Ranges in South Australia (Fig. 3). It might be interpreted as an upwelling in the upper mantle and because of its close correspondence with the seismically active zone, one could speculate that this represents the nascent stage in the development of a rift. The second array experiment has revealed a highly conducting zone in western Victoria, which may correlate with the Recent activity of the Newer Volcanics—possibly the remnant of a magma chamber at elevated temperatures.

New Development

Geology departments in the foundation universities in each of the state capital cities have been for many years the mainstay of undergraduate teaching and research in geology in Australia. With the rapid expansion of the number of universities during the past 20 years (there are now sixteen in Australia, including three in each of Sydney and Melbourne) the tendency in the newer universities has been to adopt the style Department or School of Earth Sciences following trends elsewhere. This reflects the recognition that the study of geology and of the Earth in general has developed so widely that it encompasses also geochemistry, geophysics and oceanography from the study of which much of the so-called revolution in the Earth sciences has evolved. Indeed many of the significant discoveries leading to this revolution were made in some of these institutions.

In 1972 the Australian National University in Canberra announced the establishment of a Research School of Earth Sciences in its Institute of Advanced Studies. This event marks a major advance in Earth science research in Australia and reflects the importance that the country attaches to such a development in the national interest. The Research School of Earth Sciences was created on July 1, 1973 with the appointment of Professor Anton L. Hales as its first director. Professor Hales was formerly Director of the Bernard Price Institute for Geophysical Research, Johannesburg and more recently Director of the Institute of Geological Sciences at the University of Texas at Dallas.

The Institute of Advanced Studies at the Australian National University was created as a national centre for research and postgraduate training in research soon after the Second World War. Under the guidance of Professor J. C. Jaeger (from 1952 until his retirement in 1972), the department of Geophysics and Geochemistry expanded progressively into new fields of Earth science research in which it achieved international prominence. By 1972 there were twenty-two academic staff and a comparable number of PhD students in the department engaged in a large variety of research programmes. These programmes form the nucleus for the new Research School of Earth Sciences which will expand to an ultimate size of about seventy academics in the next 15 to 20 years.

Research in the new school will concentrate on several main areas. The already existing activities in geophysics and geochemistry will be strengthened. These include investigations of the large scale geophysical structure, not only of Australia, but also of the entire Earth. Key fields in geophysics are seismology, palaeomagnetism and geomagnetism in its broadest sense (including geomagnetic deep sounding) geothermy and theoretical geophysics. Fundamental laboratory investigations relating to the crust and interior of the Earth include studies in rock deformation and the physical properties of rocks and minerals at high temperatures and pressures. Geochemical activities will continue to be concerned with the origins and ages of rock systems, evolution of the Earth's crust, the internal constitution of the Earth, the chemistry and mineralogy of lunar rocks and meteorites and chemical prob-

New developments will include fundamental research in economic geology directed towards the origin of metalliferous ore deposits, including especially studies of the physics and chemistry of ore-forming solutions and their precipitation. Not only have these subjects considerable intrinsic scientific significance, but also they have the greatest importance in the light of Australia's mineral resources. Consequently this development has the highest priority of the proposed new activities.

The initial developments in the solid Earth sciences outlined above will be complemented by expansion into the fluid Earth sciences. These will include geophysical fluid dynamics, involving especially examination of the circulations and interactions of the Earth's oceans and atmospheres. This is a subject particularly in need of study in the southern hemisphere generally and in the neighbourhood of Australia particularly. The discipline would also include problems of circulation in the Earth's liquid core and associated magnetohydrodynamics, as well as problems such as convective motions in the Earth's mantle. Studies in environmental geochemistry will be an interdisciplinary field embracing chemical interactions between the atmosphere, oceans and solid Earth, palaeoclimatology and the problems of photochemical air pollution and pollution in the hydrosphere and atmosphere.

Contribution

All these studies are of course related to the processes by which the Earth took on its present shape. Taken together these programmes should make a significant contribution to the understanding not just of the past history of Australia, its structure and environment, but of global geology and geodynamics in general.

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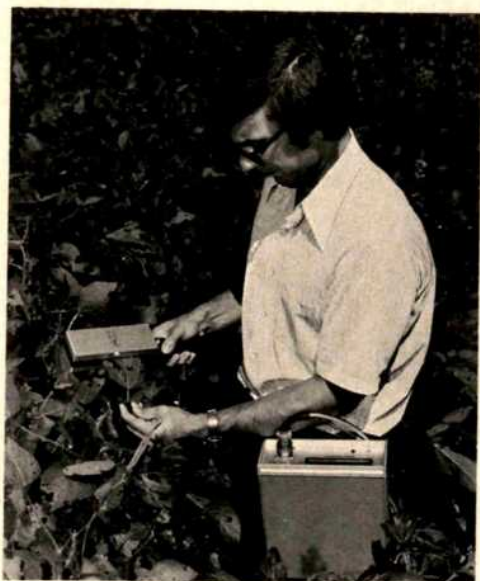
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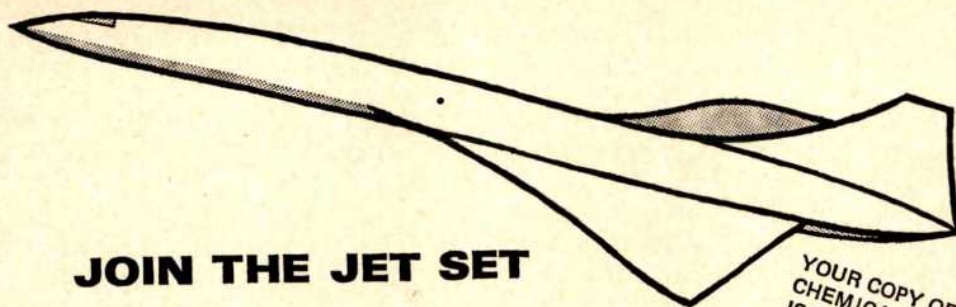
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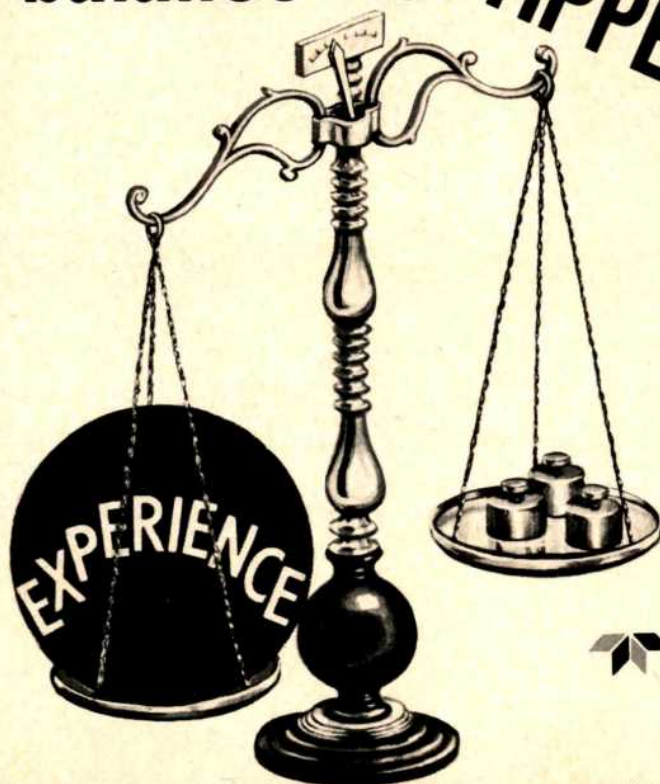
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Pest Management in Australia

D. F. WATERHOUSE

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The aim of pest management is to manipulate or manage pest populations by a combination of all available means so that they do not cause economic damage.

AUSTRALIA differs from other major land masses in that, almost without exception, its domestic animals and crop plants have been introduced from other countries. About half of its 600 most important insect pests and most of its weeds have also been introduced, often without the natural enemies which are so important in helping to suppress them in their native lands. It follows that the introduction and establishment of the most valuable of these natural enemies—the process known as biological control—is likely to be of special value to Australia. Indeed, the world's best known examples of successful biological control are the use of the *Cactoblastis* caterpillar against prickly pear and the myxomatosis virus against rabbits in Australia.

As in many other countries after the Second World War, the use of the new synthetic organic insecticides permitted a level of pest control never before attained. For a decade or more extensive resources were devoted to developing an improved insecticide technology and comparatively little emphasis was placed on the alternative means of control that had been the mainstay of earlier economic entomologists. As elsewhere, disadvantages of the use of insecticides gradually became evident, such as outbreaks of secondary pests and the appearance of strains of pests that were resistant to one or more of the pesticides used against them. Somewhat later, concern arose over unintentional effects on man and other non-target organisms.

Intuitively at first, and then as a deliberate policy, steadily increasing attention has been paid to as many as possible of the older, non-insecticidal approaches to pest control as well as new methods that have emerged more recently. The aim has been to manipulate or manage pest populations by a combination of all available means, so that they remain below the level at which they cause economic damage—hence the term 'pest management'. Insecticides are integrated into the control procedures where their advantages outweigh their disadvantages, as they often do, but it is clearly desirable to make as much use as possible of methods that do not require the continuous energy input involved in insecticide manufacture and application. Such methods are not without their own problems in the transition from complete reliance on broad spectrum pesticides to a more selective usage and at minimal dose rates necessary to produce the required result. Finally, it is important to recognise a major change that has occurred over the past 25 years. This is the extremely high (perhaps unnecessarily high) standard of freedom from insect damage that is now demanded by consumers, a standard that is far less readily achieved by non-chemical measures.

A few of the interesting projects being undertaken by Australian entomologists are described in the following thumbnail sketches, the brevity of which should not be allowed to conceal the very large effort involved in the necessary detailed studies of the ecology, population dynamics, tax-

Cattle Tick

Boophilus microplus is a serious pest in tropical and subtropical Australia, where it infests some 9 million cattle and causes losses probably exceeding A\$40 million per annum.* Until 1947 the only control practised was to dip cattle in vats containing an arsenical solution, but a new era dawned with the advent of DDT and its use became widespread and even mandatory in areas where arsenic-resistant ticks had become a problem. A little more than a decade later the use of DDT was prohibited when the residues in cattle tissues became unacceptable in overseas markets. Chemical control now depends on materials that leave low and less persistent residues. Meanwhile the tick has developed resistance to all of the materials that have ever been used against it for any appreciable period. Thus Queensland is infested by nine strains of ticks with various spectra of resistances to organophosphorus compounds and carbamates and there seems to be little prospect of any chemical remaining useful indefinitely.

To circumvent the problems of resistance and residues, considerable effort has been put into research to reduce or eliminate the use of acaricides. Two of the approaches have given particularly valuable results. (i) Studies on the duration of egg development and of the longevity of larvae waiting in the pastures for hosts showed that, although a few larvae survived for eight or nine months after the engorged parent female had fallen from the host, the majority perished within a month or so of hatching. Thus it is possible to avoid heavy tick infestations by a routine of 'pasture spelling'—vacating paddocks for periods long enough to ensure that most tick larvae have died—then restocking with cattle, which, if necessary, have been freed of ticks by dipping. Many fewer dippings are required under such a regime. (ii) The second, and by far the most valuable means of long term tick control, for it also helps to control tick fever, is the use of tick-resistant cattle. Prominent in this approach is the use of Asian breeds that have evolved in evolutionary association with the cattle tick and are resistant to tick infestation. Hybrids between such stock and European breeds make good beef animals and are often so inhospitable to ticks that dipping is unnecessary. Relatively tick-resistant animals also occur sparingly in several breeds of European origin and these have been selectively bred to produce tick-resistant herds without infusion of Asian blood, but the process is very much slower.

Sheep Blowfly

The attack on living sheep by maggots of *Lucilia cuprina* costs Australian producers at least A\$30 million a year. Infestations occur chiefly in the wrinkly crutches of merino ewes but also, when conditions favour the fly, on the shoulders and occasionally on other parts of the body. As with the cattle tick, chemicals have been used extensively for protection, but the fly has become resistant first to cyclodienes and, in more recent years, to organophosphorus compounds, and the problem of residues in carcasses limits the choice of alternative insecticides. Of older methods tried, biological control and trapping have proved to be of negligible value, and the destruction of carcasses ineffective because most of the *L. cuprina* population breeds on living sheep; susceptibility to both crutch and body strikes could be reduced by selective breeding, but nearly always at the cost of fleece production; and the one economically practicable method that would give almost complete, life-long protection from crutch strike—surgical removal of

wrinkles and correct docking of tails of young lambs—has failed to find the extensive favour among graziers that it deserves. Clearly, a new approach is needed.

In spite of the cost of the fly to the sheep industry, the cost-benefit ratio of a sterile male eradication programme, such as has been successful against the screw-worm fly in parts of the United States, is highly adverse on account of the huge area (more than one-third of Australia) infested by the pest. A cheaper method is now being investigated—the production of synthetic strains of flies with chromosomes rearranged so that they are incompatible with the chromosomes of 'wild' flies, with the result that any crosses produce non-viable progeny. Extensive genetical studies that have already been done in the laboratory show that *L. cuprina* is well suited to this approach.

Sirex Wood Wasp

Pinus radiata is by far the most important plantation softwood in Australia. In the middle forties a consignment of infested pine logs from New Zealand led to the establishment of a European wood wasp (*Sirex noctilio*) in stands of this pine in Tasmania and Victoria. Although *Sirex* wasps are of minor significance in Europe, except when pines become unthrifty or are damaged, this wasp killed many trees in New Zealand and 40% to 50% in the early years after its establishment in a plantation near Hobart.

Sirex noctilio females commonly drill several tunnels into the timber at each oviposition site, in the process introducing a toxic mucus produced in a special gland. Even minute quantities of this mucus produce a severe, temporary setback to the tree, reducing its capacity to wall off *Sirex* eggs and the associated fungus (*Amylostereum areolatum*), known only from trees into which *Sirex* has inoculated it during oviposition. Its metabolites are capable of killing the pine tree. Initially, the rapidly growing fungus helps to produce conditions in the wood suitable for the development of the newly hatched *Sirex* larva and continuity of transmission is ensured by the female taking up a fungal culture into a special pouch, the mycangium, when she emerges from the pupal skin.

Wasp parasites of the egg or young larva (*Ibalia* spp.) locate their hosts by detecting the short chain metabolites produced by the young fungus. Later a different group of wasps (*Megarhyssa* spp., *Rhyssa* spp.) locate the larger larvae deeper in the trunk by different metabolites produced by the older fungus and associated micro-organisms. Success has been realised in establishing in Australia eight wasps from various regions of the northern hemisphere, including regions where *S. noctilio* does not occur, because they use the same fungal metabolites to locate their prey. In regions of Tasmania where the complex of parasites has been longest established, attack, especially by *Megarhyssa nortoni* (Fig. 1), now exceeds 75%.

More recently, a nematode (*Deladenus siricidicola*) has also been established. Eggs of nematode-infested *S. noctilio* females consist of a chorion packed with juvenile nematodes. After oviposition these juveniles escape from the egg and enter a free living phase, feeding exclusively upon the *Sirex* fungus, moving extensively through the timber, and passing through many successive cycles of multiplication. If these free-living forms locate a *Sirex* larva, infective forms are next produced which penetrate the *Sirex* cuticle. They multiply prolifically shortly after pupation and pack into the developing eggs of the female. Most of the *S. noctilio* emerging from nematode-infested trees contain *D. siricidicola*. It is expected that the combined attack of the nematodes and the parasitic wasps will reduce the major threat that was posed by *S. noctilio* and will result in a level of attack similar to that in the northern hemisphere. The intricate relationship between the *Sirex* wasp, its specific fungus and the *Sirex* parasites is indeed unusual.

In addition to biological control, various silvicultural means have been adopted to reduce susceptibility of the pine trees. These include the selection of sites where the pines will grow vigorously, avoidance of pruning during the *Sirex* flight season, and programmed thinning to keep the trees growing vigorously.

Orchard Mites

Organophosphorus insecticides, such as azinphos methyl, give excellent control of codling moth (*Cydia pomonella*) in apple orchards in south-eastern Australia, but they produce another spectacular effect, namely the release from predator control of the two-spotted mite (*Tetranychus urticae*) which causes severe damage to the apple leaves, necessitating the application of acaricides. A predatory phytoseiid mite (*Typhlodromus occidentalis*), resistant to azinphos methyl, was introduced from the United States and is giving excellent control of the two-spotted mite in sprayed orchards.

Skeleton Weed

Skeleton weed (*Chondrilla juncea*) is an extremely serious weed in wheat fields in south-eastern Australia. Its roots penetrate deep into the soil and pieces broken off by cultivation are each capable of producing a new plant. A flat rosette of leaves is formed in autumn which grows until early summer and then produces one or more tough, flowering stems. The early growth of the weed in wheat fields rapidly depletes the surrounding soil of available nitrogen and moisture, thereby suppressing nearby wheat plants. Later the wiry stems interfere seriously with harvesting machinery. The yield of heavily infested fields can be reduced from 30 bushels per acre to 15 or less and annual losses are estimated to exceed A\$30 million.

Skeleton weed is widespread in the Middle East and Mediterranean areas, but it is a relatively uncommon plant and is hardly ever regarded as a weed. It is heavily attacked by many organisms, none of which were present in Australia when investigations commenced in 1966. Seven insects, an eriophyid bud mite and three fungi have been studied. Most destructive of the fungi was the widespread rust, *Puccinia chondrillina*, which kills young *Chondrilla* seedlings and severely damages older plants. Extensive testing of this rust against all of the plants of substantial agricultural importance to Australia demonstrated that it was entirely specific to *Chondrilla* and was quite unable to develop on other closely related Cichoriaceae. Rust spores were released in Australia in 1971, constituting the first example in the world since the establishment of effective quarantine controls, of the deliberate introduction into a new country of a plant pathogen for weed control. The rust spread spectacularly and, in less than a year, could be found infesting plants in virtually every stand of skeleton weed examined in Australia. Very extensive

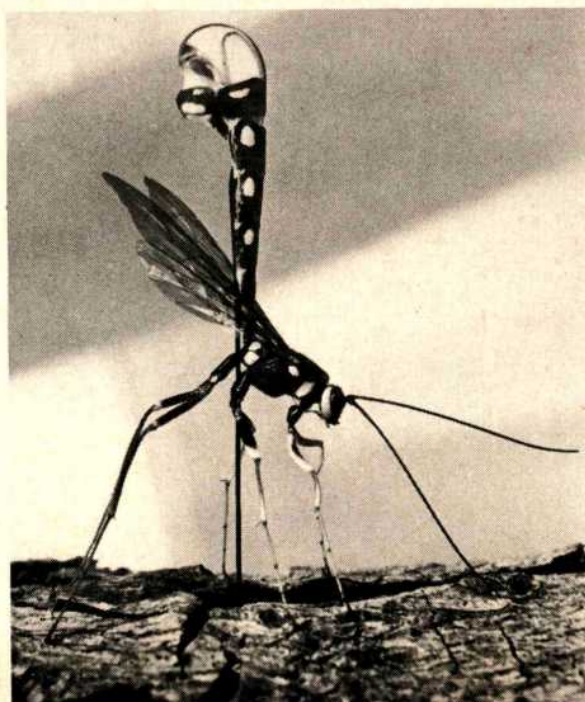


Fig. 1 *Megarhyssa nortoni* drilling in a pine log.

damage to the stems of skeleton weed plants has already occurred over vast areas, in many instances stems dying back to ground level before flowering. Vast numbers of young rosettes have also succumbed to attack. Five other organisms have so far been demonstrated to be specific to skeleton weed. Of these a gall fly, a stem-boring moth, and a bud mite have also been imported. The use of a bud mite for biological control also breaks new ground.

Potato Moth

The practicality of using an insect pathogen in lieu of an insecticide was demonstrated in large-scale field experiments against the potato moth (*Phthorimaea operculella*). A specific granulosus virus of the moth larvae was discovered and sufficient infective material accumulated to spray commercial crops of potatoes in Western Australia. One virus application at the beginning of the season was compared with the usual regular application of insecticides throughout much of the growing period of the crop. Tubers from the virus-sprayed crops were virtually free of potato moth damage, whereas there were quite high levels of damage on unsprayed crops and on some of the crops treated according to normal spray schedules. A single application of virus gave protection that equalled the best provided by insecticides. Virus-infected larvae were also discovered on untreated plots up to several miles away and insectivorous birds were found to be spreading the virus which appears to be comparatively resistant to environmental degradation. Problems of mass production and of registration as yet prevent the general use of this pathogen in commercial potato growing.

Dung Beetles

Although Australia has indigenous dung beetles adapted to dispose of the pellet-like droppings of its native herbivores, the marsupials, these beetles have negligible impact on the large dung pads of introduced cattle. Such dung pads soon dry into a hard cake where they have fallen on the pasture, many remaining substantially unchanged for months or even years. By comparison, in countries such as Africa where large herbivores evolved, the dung pads are frequently buried by beetles within a day. Bovines each produce ten or more pads a day, which continue to smother pasture until they are dispersed. Furthermore, around the periphery of each pad there develops a rank growth of pasture which cattle will not eat. In this way each bovine is capable of alienating a fifth of an acre each year and the extent of the loss can be measured by considering that there are some 30 million cattle in Australia. As well as rendering useless up to 6 million acres of pasture each year, the pads are the major breeding ground of two nuisance flies, the blood-sucking buffalo fly of cattle in the tropics and the widespread, pestiferous bush fly which worries man and other animals.

An active programme is in progress to re-establish in Australia the ecological balance whose disruption commenced



Fig. 2 *Sisyphus rubripes* rolling its dung ball.

almost two centuries ago when cattle were introduced by the First Fleet. African beetles are being introduced, using specially developed methods involving the utilisation of surface-sterilised eggs in order to prevent the introduction of any undesirable fellow travellers or diseases. Beetles of one type work in the soil directly beneath the dung pad, constructing tunnels into which they carry dung which they form into balls containing their eggs. Another type (Fig. 2) fashions dung balls which are rolled for some distance over the surface of the ground before burying. These activities reduce fly breeding and, also greatly reduce the survival of helminths hatching from eggs passed out in the dung. Some twenty beetle species have already been introduced, but it is believed that more than 100 will be required to deal with dung in all the various climatic and other environmental conditions where cow pads are abundant. Fortunately there are some 2,000 species in Africa south of the Sahara to choose from. In the 6 years since it was first liberated, one species (*Onthophagus gazella*) now buries dung pads completely in a day or so in tropical areas during the rainy season, and similarly spectacular results are being obtained with another species in northern New South Wales. If an adequate range of dung beetles is established in Australia an annual return worth many millions of dollars will unquestionably result.

In many problems, including some of the foregoing, pesticides still have a valuable role to play, but the increasing use of resistant varieties, parasites, insecticide-resistant predators, nematodes, viruses, fungal pathogens, cultural modifications and other means are all contributing to saving tens of millions of dollars each year and the prospects for further profitable extension of use of such methods are very bright indeed.

Solar Power in the Australian Energy Scene

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Dr Morse discusses the most cost effective ways of utilising solar energy in Australia and points out the possibilities of producing 'synthetic' liquid and gaseous fuels from trees and plants.

THE primary energy pattern in Australia is undergoing a very significant change due mainly to the discovery in 1966 in Bass Strait of oil and gas in commercial quantities. Prior to that the search for oil had been going on for a long time with some minor successes, but it was the Bass Strait strike which stimulated the exploration drilling which in due course led to a number of widely separated discoveries. Although these are mostly natural gas, Gidgealpa in Central Australia and the North Rankin field on the north-west

shelf off the West Australian coast will have a big influence on the national energy pattern.

Known reserves are sufficient to ensure a very important role for natural gas for the next 50 yr. Melbourne and Adelaide are already being supplied by pipelines from the Bass Strait and Gidgealpa fields respectively, and the Government has set up a Pipeline Authority to acquire and distribute petroleum products throughout Australia. It is at present arranging contracts for the pipeline to supply Sydney from the Gidgealpa field and is investigating the feasibility of supplying Perth, Kalgoorlie and the Pilbara.*

The Department of Minerals and Energy's forecast, dated August 1973 (ref. 1) for fuel consumption in 1984-85 is given in Table 1. During the period 1972-73 to 1984-85 natural gas consumption is expected to increase at 18.9% a year and by 1985 it will be supplying about 10^{18} J yr⁻¹. At this rate of consumption, published reserves will be exhausted by the year 2020.

Table 1 Forecast of Australian Energy Consumption

Fuel	Percentage of total		Annual usage $\text{J} \times 10^{-18}$	
	1971-72	1984-85	1971-72	1984-85
Petroleum products	49.5	41.8	1.111	2.166
Black coal	29.8	26.5	0.669	1.374
Brown coal	10.6	10.4	0.237	0.540
Natural gas	4.5	18.5	0.102	0.956
Bagasse	2.0	1.2	0.045	0.060
Hydroelectricity	1.9	1.1	0.042	0.058
Wood	1.7	0.5	0.038	0.023
Total	100	100	2.244	5.177

Indigenous oil reserves are much less and according to recent announcements by the Minister for Minerals and Energy will be exhausted in about 8 yr. Imports of liquid petroleum products, which are at present about one-third of the total, can therefore be expected to increase steadily during the next decade unless there are new discoveries. Since these account for nearly 50% of Australia's present primary energy requirements, this situation has far-reaching implications. More than half is used for transportation, which has become increasingly dependent on liquid fuel. It is expected that in the near future about one-third of the nation's total primary energy will be used for transportation, most of which is required in the form of liquid fuel.

Australian coal reserves are very large and provide the primary energy for 75% of the country's electric power production, the remaining 25% being hydroelectric. Since future hydroelectric development will be limited, the nation's electric power system will become increasingly dependent on thermal stations operating on both black and brown coal. A natural gas-fired power station is planned for Melbourne but there are no nuclear power plants either in operation or under construction.

A summary of known recoverable energy sources prepared by George² is given in Table 2, with some updating for natural gas. The enormous energy recovery from uranium using breeder reactors has focused attention on the problems of nuclear power generation, particularly the difficulty of disposing of radioactive wastes. The risk of

irreversible genetic damage to plant and animal life on a large scale has stimulated the study of alternative power sources which have a low environmental impact.

A comparison of the numbers in Tables 1 and 2 shows that Australia has ample reserves of both black and brown coal to supply its power stations for a very long time to come and is therefore in the fortunate position of being able to defer a decision on the introduction of nuclear power until the waste problem has been satisfactorily solved.

In the meantime there is growing interest in the development of renewable energy sources which are 'clean'. The ultimate hydroelectric development is about double the present capacity. The tide range of the north-west coast, extending about 1,000 mile west of Darwin, is typically 10 to 12 m, which has provided the basis for suggestions that tidal power could have a large potential in this area. Wind power may have useful applications on a small scale in specific areas but is most unlikely to make a significant contribution on a national scale.

Solar Power

There is, however, now widespread recognition of the potential of solar energy as a future major power source for Australia, and some of the implications were considered at a UNESCO symposium in Adelaide in May 1973 (ref. 3). A Committee appointed by the Australian Academy of Science has suggested targets for the contribution of solar energy to the nation's primary energy needs and recommends a substantial programme of research⁴.

Already there is a small but efficient solar water heating industry producing well engineered absorbers, and about 20,000 m² have been installed throughout the country. They provide heat at about 60° C and are suitable for manufacturing, commercial and residential applications. This industry is backed by a research programme in the CSIRO's Division of Mechanical Engineering and several of the Australian universities, which have been studying the use of solar energy in the form of heat at low temperatures. This work is being extended to include applications up to about 120° C, embracing the industrial use of low pressure steam. It seems that the heat required at these temperatures accounts for about one-third of the total primary energy used and is the most promising area for solar energy utilisation at the present time.

Solar energy is widely and fairly evenly dispersed and is generally available where it is needed without reticulation. The annual insolation on a horizontal surface does not vary very much throughout Australia (Fig. 1). The Simpson Desert, for example, collects only about 30% more solar energy than Melbourne. Places near the Equator have the advantage, however, that variations in insolation from season to season are small, so that solar-powered devices can operate more efficiently. For Darwin, latitude 12° S, the mean daily insolation collected on an inclined surface in the best month is only 40% more than the worst month, whereas for Melbourne the difference is 120%. This means that solar water heaters in Darwin can operate satisfactorily without fuel or electric boosters but in Melbourne they cannot.

Solar radiation consists of a direct and diffuse component. Diffuse radiation is due to scattering in the Earth's atmosphere, and arrives on a horizontal surface approximately uniformly from all directions in the sky. It is typically between 20 and 40% of the total energy received in a year and this is lost when solar energy is concentrated by a focusing collector. The popularity of the flat plate absorber is due to its simplicity and its ability to collect both diffuse and direct radiation in a fixed position. Concentration can only be justified when high temperatures are required, and it seems that the most effective way of using solar energy is to collect and use it at low temperatures.

Table 2 Summary of Australia's Known Recoverable Energy Resources

		Gross energy equivalence $\text{J} \times 10^{-18}$
Black coal	12,601 million ton	300
Brown coal	20,000 million ton	200
Oil	2,110 million barrels	10
Natural gas	34×10^{12} foot ³	36
Uranium	142,000 short ton	60
	or with breeding	6,000

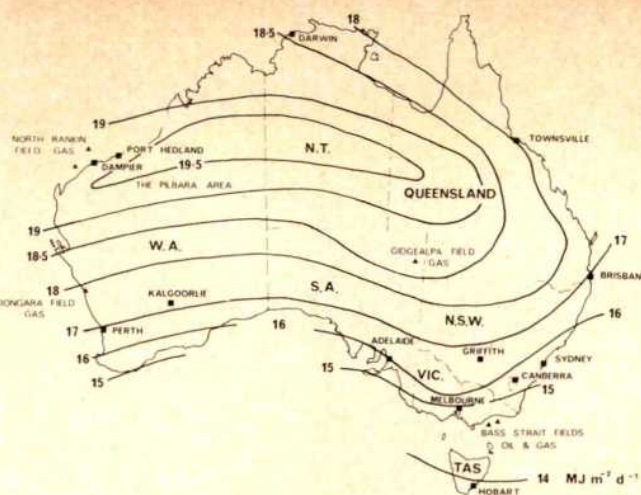


Fig. 1 Average daily solar radiation on a horizontal surface over Australia. Source: CSIRO Divisions of Atmospheric Physics and Mechanical Engineering.

A well designed commercially produced solar water heater⁵, comprising absorbers and insulated storage with thermo-syphon flow connections, has an overall efficiency of 40%, expressed as the ratio of the annual quantity of heat available in the tank to the total radiation incident on the absorber over the same period. This is remarkably high compared with, say, a silicon cell (18%) and photosynthesis in plants (0.5%). It illustrates a basic characteristic of effective solar energy utilisation, which is that special purpose devices are used to perform specific functions, for example, water heating, desalination, drying and electric power. It would be very wasteful, for example, to generate electric power at 10% collection efficiency, feed it into a distribution network and then use the electricity to heat water.

It is now widely accepted⁴ that the most immediately effective way in which solar energy could supply some of the nation's energy needs would be in the form of low grade heat at temperatures up to about 120° C, and that research and development are needed to improve the cost effectiveness of installations for domestic, industrial and process water heating, house, factory and office heating, food processing, drying, desalination and possibly comfort cooling.

The cost effectiveness of a solar installation can be expressed as a figure of merit or a return on investment due to the value of the fuel saved, and techniques have been developed to optimise this⁶. It is dependent on many factors, including fuel cost, temperature at which the heat is required, and the proportion of the annual heat requirement which is to be met by solar energy. In general terms, the return on investment is high at low collection temperatures and where the percentage solar contribution is low, and decreases for higher temperatures and high percentage solar contribu-

tion. Accordingly the most attractive way to utilise solar energy now may well be to install solar absorbers sufficient to supply 20 to 30% of the annual fuel needs, and subsequently increase the collection area as fuel costs rise and so maintain a gross return of, say, 15% per annum on the solar investment. There are, however, favourable situations, such as Darwin, where a 100% solar water heating system at 55° C can return 30% per annum on the solar investment. Generally it will be necessary to use a solar plus fuel-booster system to achieve an acceptable figure of merit.

Although solar energy can reduce the community's dependence on liquid petroleum fuels where these are producing low grade heat, by far the most important use of liquid fuels is for transportation. Here there is the intriguing possibility of the production of a synthetic fuel from cellulose, which can be considered as solar energy which has been stored in trees and plants. Both liquid and gaseous fuels can be produced from cellulose and other plant material by known processes. These processes have not yet been used on a large scale and considerable research and development will be needed before their practicability can be evaluated. It seems, however, that an area of 5×10^6 ha, that is, less than 1% of Australia's land area, would be adequate to provide 10^{18} J yr⁻¹ as a liquid fuel on a perpetual cycle. In this way the CO₂ which is produced when the fuel is burnt is recycled by photosynthesis in the plants. This is such a challenging objective that it is sure to be studied in considerable detail.

The generation of electric power from solar energy using photovoltaic, thermoelectric or thermodynamic processes is a less attractive proposition than either the low grade heat or synthetic fuel applications. It suffers both on the score of cost effectiveness and technological feasibility. There are no practicable large scale solar electric power plants in operation or even in sight at present. Australia's large coal reserves will defer the need for alternatives to conventional power generation for a considerable time. Photovoltaic devices, like the silicon cell at present very expensive, should drop substantially in cost over the next two or three decades, and may well be suitable for use in isolated areas where reticulation from central power stations is inherently costly. In fact, this could be one of the long term advantages of solar energy: its availability where it is required without reticulation.

It has been suggested⁴ that by the year 2000 solar energy could be an important primary energy source for Australia, providing 10^{18} J yr⁻¹ in the form of low grade heat and another 10^{18} J yr⁻¹ as synthetic fuel. If this is to be achieved it would involve the creation of a major new industry, as well as substantial research and development by government, academic and industrial laboratories. It is not possible to say yet whether the economic incentives resulting from the anticipated cost increase in naturally occurring fuels will be sufficient to bring this about, or whether it will be necessary or even desirable to introduce other incentives. The prospect, however, of a quarter of Australia's primary energy coming from a renewable source within 30 yr is one which has to be taken seriously.

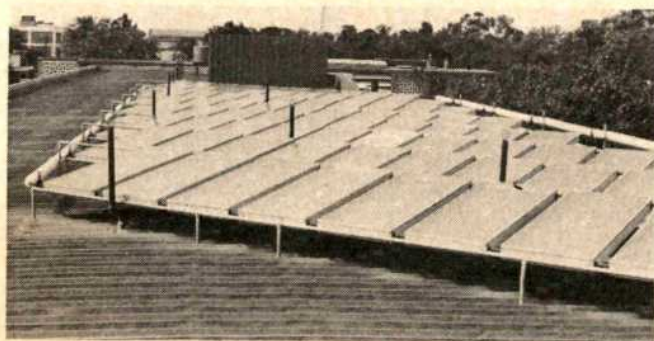


Fig. 2 Solar water heating installation on the roof of the Esplanade Hostel, Darwin.

¹ *Forecast Consumption of Primary Fuels 1972/73 to 1984/85* (Fuels Branch, Department of Minerals and Energy, Melbourne, 1973).

² George, D. W., *Energy resources and usage*, Charles Kolling Research Laboratory Technical Note ER-2 (University of Sydney, 1973).

³ Morse, R. N., *Proc. UNESCO Man and the Biosphere National Symposium on Energy and How We Live* (Flinders University, Adelaide, 1973).

⁴ *Report of Committee on Solar Energy Research in Australia* (Australian Academy of Science, 1973).

⁵ *Solar Water Heaters—Principles of Design, Construction and Installation*, CSIRO Division of Mechanical Engineering Circular No. 2 (1964).

⁶ Morse, R. N., Davey, E. T., and Welch, L. W., *High temperature solar water heating*, paper EH60, *Proc. int. Cong. "The Sun in the Service of Mankind"* (Paris, July 1973).

Rock Art in Australia

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A national programme of recording of Aboriginal rock art sites has been accepted by the Australian Institute of Aboriginal Studies as one of its principal research priorities.

ABORIGINAL rock art in Australia has engaged the interest of European explorers and settlers since they arrived in the continent in 1788. Many of the observations made, and questions asked by them, remain as pertinent today as they did then. For example, Grey¹ was concerned with establishing dates for the art which he found in the Kimberleys: "With regard to the age of these paintings, we had no clue whatever to guide us. It is certain that they may have been very ancient, for although the colours were composed of such perishable materials, they were all mixed with a resinous gum, insoluble in water, and no doubt, when thus prepared, they would be capable of resisting, for a long period, the usual atmospheric causes of decay. The painting which appeared to me to have been the longest executed was the one clothed in the long red dress, but I came to this conclusion solely from its state of decay and dilapidation, and these may possibly have misled me very much".

In addition, the early history of the discoveries, and the statements made by the first Governor of Australia, Arthur Phillip², could, and we believe should, have had a profound impact on the doubtful assumptions and assertions made in connection with the acceptance of some rock art of prehistoric Europe as archaeologically ancient and as the work of hunters and gatherers. In 1788, within 3 months of setting foot in Australia, Phillip, while on one of his first explorations near Sydney, found a series of rock carvings. He wrote²: "... in the neighbourhood of Botany Bay and Port Jackson, the figures of animals, of shields, and weapons, and even of men, have been seen carved upon the rocks, roughly indeed, but sufficiently well to ascertain very fully what was the object intended ... that the arts of imitation and amusement, should thus in any degree precede those of necessity, seems an exception to the rules laid down by theory for the progress of invention. But perhaps it may better be considered as a proof that the climate is never so severe as to make the provision of covering or shelter a matter of absolute necessity". In Europe, it took from 1878 to 1902 for scholars to accept the great antiquity of Palaeolithic art and thus, implicitly at least, to overcome the generally held assumption that hunters and gatherers could not have had the time, and were by definition, incapable of producing art works³. Even as late as 1966 the main message emanating from an international conference⁴ on hunters and gatherers was that foragers were not totally preoccupied with the quest for food. In Australia there has never been any doubt that hunters and gatherers had the time, capacity and motivation to carry out works of art.

Overall, the work of the early explorers and colonisers of Australia, in so far as it concerned Aboriginal culture and rock art, was largely objective recording and description and, at the same time, showed a depth of enquiry and perception well ahead of much scientific enquiry in other continents concerned with hunters and gatherers.

Acute descriptions, such as those of Grey¹ in the Kimberleys—"Each of the four faces was marked by a totally

distinct expression of countenance, ... although none of them had mouths ..."—and King⁵ on Clack's Island—"They were executed upon a ground of red ochre and were delineated by dots of white ... earth (and) decorated all over ... in dotted transverse belts"—serve to distinguish different Aboriginal rock art styles.

Distribution and Age

During the late nineteenth century enlightened amateurs carried on sporadic recording and observations. No significant advances regarding the identification of stylistic variation in Aboriginal art took place; indeed the assumption of the time was, as Mathews⁶ wrote: "Aboriginal drawings are almost everywhere of the same character, with but little variation either in the subjects treated or in the style of workmanship." The main change in approach to the systematic analysis of Australian rock art started with the impetus of the ethnographic recording of Spencer and Gillen⁷. Their work placed emphasis on the material culture and rich ceremonial of Aboriginal life, and focused attention on the contemporaneity of Aboriginal culture. Basedow's work⁸ provided a corrective to the synchronic study of Aboriginal culture and art: "The conclusion is that some of the Australian designs must, upon this evidence alone, be regarded as extremely old." Basedow, in addition, reviewed a large body of material in order to reach conclusions about Aboriginal rock art styles and techniques. This approach continued in the work of pioneers of the scientific study of Australian rock art such as Mountford⁹, Davidson¹⁰ and McCarthy¹¹.

Much of the work of the authorities just mentioned took place during the time that archaeology began to develop in its own right. Research of this kind aimed at both detailed recording of rock art sites, the widening of knowledge of the geographic distribution of Aboriginal art works and the definition of 'styles', and more particularly techniques. McCarthy¹², in addition, initiated the numerical expression of the contents of the elements making up Aboriginal rock art. Such work, undertaken by a few dedicated people at a time when the analysis of rock art was not recognised as part of



Fig. 1 Finger marks on the soft wall surfaces in Koonalda Cave, South Australia.

academic university studies, formed the basis of research on Australian Aboriginal art until a few years ago.

During the past ten years or so the picture regarding not only the wide distribution and the complexity of styles but also the antiquity of Aboriginal rock art has changed fundamentally. The first possible indication of the real age of rock engravings came as early as 1929, with the discovery¹³ of abraded grooves on the back wall of the Devon Downs rock shelter on the lower River Murray at a depth of between 3 and 4 m below ground surface. It was not until 1966, however, that a positive date was obtained for engravings. The site was a shelter adjacent to the permanent Ingaladdi waterhole on Willeroo Station in the Northern Territory. The walls of the sandstone outcrop were covered completely with engravings and paintings. Many engravings were weathered and strongly patinated, but others, including one of a ship, were obviously of recent origin. Detached rock fragments bearing engraved bird and animal tracks and abraded grooves were found in the main excavation trench. These engraved pieces were recovered between levels radiocarbon dated to $4,920 \pm 100$ BP and $6,800 \pm 270$ BP¹⁴.

A year later, at Koonalda Cave on the Nullarbor Plain in South Australia, charcoal from a passage deep down in the cave yielded a date of about 20,000 BP¹⁵. The charcoal could have come from crude torches used by prehistoric man, who came to the cave to mine flint. For the first time in Australia, a site contained evidence of artistic activity carried out in total darkness inside a deep cave. The 'art' consisted of finger impressions (Fig. 1) in the soft and friable walls, and incised lines abraded or scratched into the harder surfaces. Although there was no direct association between engravings and charcoal, the fact that large areas of engravings were found in a cavity 15 m below a rock fall confirms the 20,000 yr date for the art¹⁶.

Rock engravings in Tasmania had been known since the 1930s, but it is only very recently that new sites have revealed the extent of this art form and provided an adequate sample for comparative analysis. The engraving technique used is



Fig. 2 Drawings made by Grey in 1838 of Wandjina cave paintings in Western Australia.

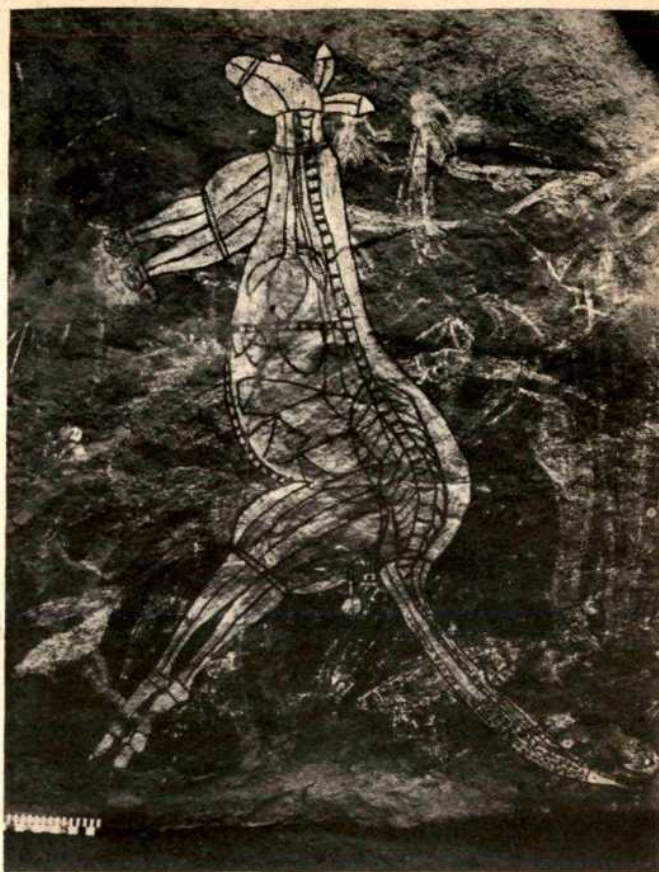


Fig. 3 Kangaroo painted in X-ray style with backbone and internal organs depicted, Arnhem Land.

identical to that found over a wide area of the mainland and the motifs also are known from many sites. It seems likely that these similarities are evidence for a common artistic tradition between Tasmania and other parts of Australia. If this is so the art must date back to a period of at least 12,000 yr, before the time that Tasmania was separated from the mainland¹⁵.

In assessing the antiquity of painting in rock shelters unfortunately one has to rely on the dating of ochre found in excavation deposits. Ochre pieces with ground facets have been found in many sites, extending back some 19,000 yr at Kenniff Cave and two sites in Arnhem Land and 30,000 yr at Mungo¹⁵ (and personal communication from D. J. Mulvaney and J. Kamminga). If the ochre was used for rock art as well as for body painting and decoration of material objects it would seem that rock paintings had at least as great an antiquity as rock engravings. Rock art in Australia is therefore at least as old as art anywhere in the world.

Styles of Art

The analysis of rock paintings has focused mainly on the definition of styles and the recognition of artistic regions. The Wandjina figures (Fig. 2) of the Kimberleys of Western Australia¹⁷, unique in terms of their large size, absence of mouths and various other attributes, remain, as already noted by Grey¹, distinctive and restricted geographically.

X-ray art, first described in Arnhem Land by Spencer¹⁸ in 1912 (Fig. 3), is a particular art form through which the Aborigines portrayed features in excess of those which are externally visible; X-ray art is now known to extend at least throughout the whole of Arnhem Land. Another identifiable form is the so-called *Mimi* art of Northern Australia¹⁹ in which human 'stick' figures are depicted with attenuated limbs and are usually shown full of animation. In the centre of Australia the engravings and paintings are based on a restricted repertoire of lines, circles, tracks and geometric motifs²⁰. Over most of south-eastern Australia the art is concerned with

The recent discoveries by Trezise²² of the vast art complexes of the Laura area of Cape York in Queensland have revealed a distinctive complexity and richness of representations of local flora and fauna, artefacts and anthropomorphic and other beings, hitherto unsuspected in the continent of Australia. Some paintings in this region could date back 10,000 yr, as ground ochre was found throughout a deposit in a decorated rock shelter²³. Stencilling¹¹, at least of hands, seems to be present throughout Australia; stencils of feet and objects of material culture may have been more limited geographically (Fig. 4).

The vastness of the Australian continent, the inhospitable nature of much of the terrain and the real practical difficulties of carrying out field work, explain in part what is perhaps the chief reason for the incomplete nature of knowledge of the distribution and characteristics of Aboriginal rock art.

Present and Future Research

During the past ten years or so some 100 decorated new sites have been found. As a consequence of the increasing realization of the importance of adequate scientific recording of Aboriginal art and of the major significance attached to various of these sites by living Aborigines, a national programme of recording has been initiated by the Australian Institute of Aboriginal Studies. Some twenty fieldworkers have been employed on a full-time basis for an initial 5 years in order to plot and record art sites throughout the continent. A growing realisation of the importance of Aboriginal art in the world context, and equally of the complexity of adequately documenting it, has led the institute to accept as one of its major research priorities the analysis in depth of Australian rock art sites. What is envisaged is the cooperative undertaking, by international experts, of the recording of particular rock art sites or areas of artistic activity, with a view to:

- The documenting, with the aid of Aboriginal informants, of the reasons and influences which underlie current artistic activity.
- The recording of Aboriginal rock art sites in the greatest detail possible.
- The precise definition and analysis of styles, content and antiquity of Australian rock art.
- The quantitative recording of the content of the art.

Techniques, such as photogrammetry, which for practical reasons in the context of European Palaeolithic art inside deep caves have proved unsuitable, have just begun to be used in Australia for recording the art in rock shelters.

Interest in the study of Aboriginal rock art has, for many decades, been focused on its relevance to prehistoric art in other continents³. It is clear that this orientation should not be

the sole reason for such research and analysis, but nevertheless there is no doubt that the Australian situation is unique as, in some regions, Aborigines continue not only to value their rock art sites but also to maintain their artistic activities and, where appropriate, their associated ritual. Immediate research in Australia will focus on documenting the 'explanations' and details which Aborigines are able to give regarding their rock art.

In 1895 Mathews²⁴ wrote: "The painted and carved rocks of Australia, the handiwork of the Aboriginal inhabitants, are widely scattered over the continent, and it is a matter of surprise that a subject of so much interest and value to anthropologists should have been so long neglected by scientific men, and others, competent to deal with them. It is greatly to be deplored that these drawings received so little attention from early settlers in the Australian colonies, who must have had numerous opportunities of observing them, and that no efforts were at that time made to record and preserve these specimens of pictorial art, showing the imitative and inventive faculties of a primitive people"—sentiments to be echoed no less today.

The challenge to current fieldworkers is highlighted by the fact that some individuals are continuing to decorate rock surfaces and that different groups of Aborigines are returning to their lands and have revived, or are about to begin to renew, the painted art of the rock shelters. Part of the challenge for the future of the study of art in Australia is to be allowed the privilege of witnessing and recording the return to this fundamental activity. It is not long ago that rock engraving was a living art form; in the present context of Aboriginal activity, the decoration of rocks in general may survive.

Further research must also concentrate on the scientific analysis of tool marks left in the engraved designs and also on a search for tools at the engraved and painted sites. Only in this way can it be shown whether or not the artists had specialised tools devoted to engraving and what sort of activities were carried out at these sites.

Calculations of the relative frequencies of the occurrence of designs and subject matter are currently in progress²⁰. They will serve to distinguish individual from 'group' activity and will also provide a more secure basis for the objective assessment of local or regional definition of rock art areas. At present it seems that in engraved rock art sites, animal tracks and circles are represented much more frequently than all other items. Studies of orientation, relative size, complexity of figures and associations are also planned.

Work is under way to determine the physical factors contributing to the erosion and patination of rock surfaces, particularly with reference to the assessment of the length of time inherent in the formation of the various conditions which today characterise the visible rock surfaces of Aboriginal art sites and also with reference to problems of conservation. In some instances it is possible that the joint evidence of natural agents and Aboriginal attitudes towards their art and its renovation, may yield clues to the dating of particular art activity.

Another immediate priority for future research in Australia must be the attempt to date Aboriginal art activities scientifically. An important new aspect is that archaeological research is being directed to the investigation of the antiquity of art sites. Excavations will be carried out where it is likely that engraved or painted wall surfaces have been buried under habitation debris.

Priorities for research on Aboriginal rock art should be influenced by international work on similar material but they should also be determined by the particular characteristics of Australian art. An important problem is the extent, and the nature, of the factors which allow one artistic motif as opposed to another to be interpreted variously according to the operative social contexts^{25, 26}. Another problem common to studies of most rock art is the definition of 'naturalistic' and 'schematic' representations. In other parts of the world, so



Fig. 4 Stencil hands, a boomerang and stone axe, on the walls of a Cammerayem Rock shelter, Queensland.

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called schematisation has been taken as a chronological marker²⁷. Australia, with its unique opportunities for consultation with the artists concerned, as well as the time depth and complexity of the rock art, offers perhaps the best hope for the clear definition of such stylistic features.

International Significance

Not surprisingly, many of the methods of analyses, and approaches to the study of Australian rock art, are identical to those used in other areas of the world. Frequently it is not possible to prove a clear association between a work of art on a cave or shelter wall and a nearby archaeological deposit. For this reason, throughout the world, the dating of rock art has had to rely to a considerable degree on the content of the art. This is no less true of Australia where, today, much of the rock art has become archaeological material²⁸. Neither in terms of method, nor in resulting discussions, is there any difference between the way prehistorians and anthropologists have approached the identification of artistic depictions of tool and weapon types in different parts of the world. Similarly, the mammoth/elephant of the European Ice Age art and the dingo of Australian art have been seen to be critical for dating the respective rock arts and, in both cases, their positive identification in art has proved difficult. Imperceptibly, in the analysis of rock art, what seems to be a simple problem of chronology becomes a complex matter involving the observer's views regarding style and artistic licence. Furthermore, the possibility, in almost all rock art of the world, that some representations may refer to beings of mythical or 'monstrous' significance adds a further bewildering complication to the secure identification of specific representations which may be crucial for dating purposes. Dating of Australian art relies heavily on the correct identification of painted domesticated animals, guns, ships, Macassans, Chinese and Europeans.

Superpositioning of representations is again one which characterises much rock art throughout the world. There can be no doubt about the importance of the correct understanding of this practice, not only in terms of chronology but also for the understanding of the artistic activities involved in producing rock art and the interpretation of the significance of much of this art form^{3,28}. In this context there should be a general realisation, deriving from the recent analysis of European rock art by Leroi-Gourhan²⁹, of both the complexity and the extreme importance of the Australian evidence despite the fact that much of it is self-contradictory and ambiguous^{3,28}.

At first sight it is possible to list the unique qualities of content and context of Australian rock art, as compared with any other single body of rock art. But work has hardly begun on a rigorous attempt to define and make such comparisons precise and, as a result, the conceptual and analytical assumptions made in any comparative generalisations are naïve and unsystematic. It was not difficult, only a few years ago, when both the range and antiquity of the Australian material was unknown, to pinpoint the supposed difference between European Palaeolithic and Australian art; the first includes mobile art and a static parietal art concerned with animals and situated deep inside caves, and the second is without mobile works, has parietal works in the open air and is full of animated action. But to adopt such an approach is to ignore the variety of both European Palaeolithic art and the Australian evidence (for example, Palaeolithic art is found also in open air shelters and sometimes also apparently concerned with movement and action³, and Australian art now includes the evidence of Koonalda and is not uniquely concerned with scenic activities). Furthermore, almost no attempt exists at a rigorous comparison of the Australian material with the art of other hunters and gatherers; for example with the East Spanish Levantine material³², which is also an open air art of animated action.

To make meaningful statements about similarities and differences between the rock arts of different ages and widely separated areas demands fundamental re-analysis of existing material and rethinking of current assumptions about the nature of these art forms. Not the least of these concerns the significance of similar artistic modes of expression; these similarities range from 'simple' engraved lines, finger-traced meanders and hand stencils to the 'complex' X-ray representations of animals and fish. Such 'artistic parallels' should lead not only to a re-evaluation of current ideas about the likelihood and conditions under which 'simple' and 'complex' independent inventions take place, but also to a new debate about the legitimacy of regarding 'rock art' as a particular art form in its own right. Australia, with its 'living' complex of song, dance, music, ritual and rock art, offers a unique possibility to answer such questions. Furthermore, future analysis of the historical and functional relationship and interaction between Australian rock art and bark paintings, should be able to cast the first reliable light on the claim that rock art is a unique art form characterised by the artist's use of a static and 'given canvas' possessing its own particular natural qualities. Only when the answers to such problems and questions are known will it become possible to assess the legitimate 'limits of inference' to be drawn from the study and analysis of rock art.

We thank Jim Allen, John Mulvaney and Andrée Rosenfeld for comments on this paper.

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Emerging Picture of Pleistocene Australians

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Man was well established in Greater Australia between 25,000 and 30,000 years ago and by at least 20,000 BP was occupying almost all of the principal ecological zones of the continent.

WALLACEA, with its numerous water barriers, was the decisive geographical influence on the prehistory of man on the Australian continent. Not only did it stem his southwards thrust from Asia for many hundreds of millennia, but it also served to isolate those human migrants who eventually acquired the technology to cross it. The theme of Australian prehistory is one of vast cultural continuities in space and time, characterised by conservatism and punctuated only rarely by influences from outside. The continental island of Java, periodically joined to the Asian mainland during periods of low sea level, has a rich human fossil record which extends back to about 2 million years ago. Stone tools of Pajitanian type in association with several species of extinct elephants have been found eroding out of the presumed middle or early upper Pleistocene deposits on the islands of the Philippines, Flores and Timor¹, showing that these animals and man had managed to cross some substantial water straits in ancient times. There remained only one more barrier, which even during low sea levels was never less than about 40 miles wide.

Antiquity

The present evidence for the antiquity of man on the Greater Australian continent, including New Guinea and Tasmania, is shown in Table 1, where I have listed the basal radiocarbon dates for twenty-eight sites which are the oldest in their respective 'regions'; their locations are shown on Fig. 1.

It can be seen that man was well established between 25,000 and 30,000 yr ago, the oldest unequivocal evidence being the 32,000 BP date from the sand lunette bordering Lake Mungo^{6,10,16}. Older data may come from the river terrace deposits at Keilor, but the situation there is complicated by disagreement as to whether or not some of the stone and bone finds were fashioned by natural agencies rather than by human hand^{5,8,13,17}. Nevertheless, some indubitable flakes have been recovered by Gallus and his colleagues from deposits which must be at least 30,000 yr old and are probably considerably older. All the results shown in Table 1 were gained during the past decade and the pace of discovery shows no sign of abating. While the search for older sites continues, the outlines of the prehistory of man in Australia during the past 30,000 yr is also beginning to emerge.

The Lake Mungo lady, securely dated to 25,000 BP, was fully sapient, with a gracile cranium that can be fitted within the morphological range displayed by modern Australoids^{10,18}. This find, combined with remains from Niah and perhaps Tabon, shows that modern *sapiens* types were present in the south-east Asian region 30,000 and more years ago. In Australia, other morphologically 'modern' skulls are those from Keilor and Green Gully¹⁰ dated respectively to about 15,000 and 8,000 BP showing continuity to recent times. The situation is, however, complicated by the discovery of the 10,000 yr old Kow Swamp series, the crania of which show remarkably archaic characteristics for such late population⁹.

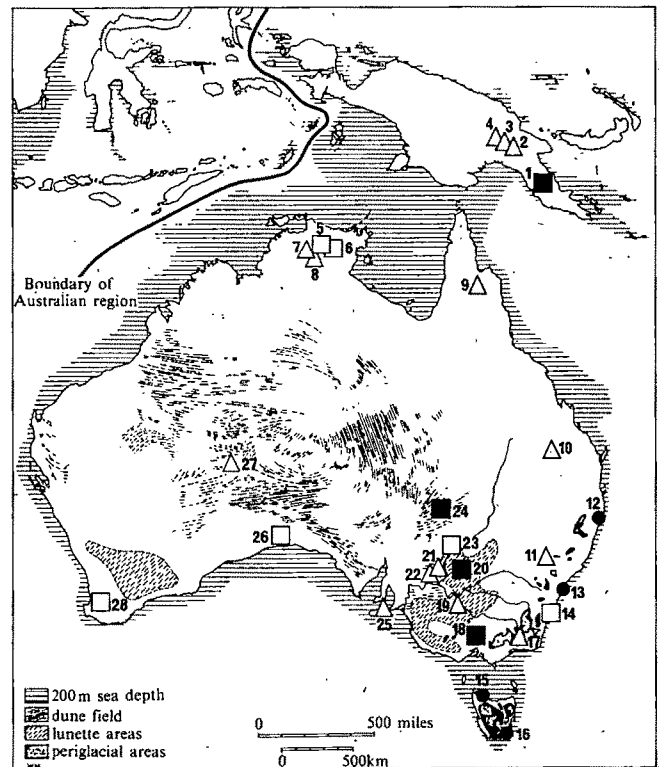


Fig. 1 Early man sites in Greater Australia. ●, Late Pleistocene; ●, 5,000-10,000; △, 10,000-20,000; □, 20,000-25,000; ■, 25,000-32,000 BP.

Many features of the facial region, such as the flat sloping foreheads, the supraorbital ridges and the massive mandibles, are reminiscent of *erectus* traits, and this tendency towards a robust form and a combination of archaic and modern features has been noted in several other late or post Pleistocene skulls such as Talgai, Cohuna, Mossgiel, and Nitchie²⁰.

The co-existence of these two groups within the same relatively small area of south-eastern Australia during a period of presumably 20,000 or more years, requires an explanation.

Table 1 Evidence of Prehistoric Man on the Greater Australian Continent

No. on Fig. 1	Site name	State	Type of site	Basal date of occupation BP	Laboratory No.	Material	Excavator	Further reference
1	Kosipe	TPNG	Open site, weathered volcanic ash	26,450 ± 880 26,870 ± 590	ANU-190 ANU-191	Charcoal Charcoal	J. P. White and B. P. Ruxton	2
2	Kafiavana	TPNG	Limestone rock shelter	>10,730 ± 370	ANU-41b	Bone 'collagen'	J. P. White	3
3	Kiowa	TPNG	Rock shelter	10,350 ± 140	Y-1366	Charcoal	S. Bulmer	3, 4
4	Yuku	TPNG	Limestone rock shelter	>9,780 ± 150 (top of deposit)	ANU-358	Charcoal	S. Bulmer	3
5	Malangangerr	NT	Sandstone rock shelter	24,800 ± 1600	ANU-77a	Charcoal	C. White (née Shrire)	4, 5
6	Nawamoyne	NT	Sandstone rock shelter	22,900 ± 1000	ANU-77b	Charcoal	C. White (Shrire)	4, 5
7	Malakunanja II	NT	Sandstone rock shelter	21,450 ± 380	ANU-51	Charcoal	J. Kamminga	Personal communication
8	Linoner site	NT	Sandstone rock shelter	18,040 ± 320	SUA-265	Charcoal	J. Kamminga	Personal communication
9	Laura	Q	Sandstone rock shelter	>19,900 ± 280	SUA-237	Charcoal	R. W. S. Wright	4, 5
10	Kenniff Cave	Q	Sandstone cave	>6,870 ± 150 (half way down deposit; base probably 10,000)	I-1735	Charcoal		
11	Noola	NSW	Sandstone rock shelter	18,800 ± 480	ANU-345	Charcoal	D. J. Mulvaney	5
12	Seelands	NSW	Rock shelter	12,550 ± 185	V-35	Charcoal	N. B. Tindale	4, 5
13	Curragurung	NSW	Sandstone rock shelter	6,444 ± 74	V-27	Charcoal	I. McBryde	4, 5
14	Burrill Lake	NSW	Sandstone rock shelter	7,450 ± 180	Gak-482	Charcoal	J. V. S. Megaw	4, 5
15	Rocky Cape, South	T	Shell midden in quartzite cave	20,760 ± 80	ANU-137	Charcoal	R. Lampert	6, 7
16	Carlton	T	Open shell midden	8,120 ± 165	Gx0-266	Charcoal	G. Reber R. Jones	4
17	Cloggs Cave, Buchan	V	Limestone cave	8,700 ± 200	I-323	Charcoal	G. Reber	4
18	Keilor	V	River terrace deposits	17,720 ± 840	ANU-840	Charcoal	J. Flood	Personal communication
18	Keilor	V	River terrace deposits	>18,000 ± 500	NZ-207	Charcoal	E. Gill	6, 8
19	Kow Swamp	V	Lakeside lunette dune	>31,600 + 1,100 - 1,300	ANU-65	Charcoal	A. Gallus	4, 5, 6, 8
20	Lake Mungo 2	NSW	Lakeside lunette dune	10,070 ± 250	ANU-403b	Bone 'apatite'	A. Thorne	9
20	Lake Mungo 3	NSW	Lakeside lunette oven	32,750 ± 1250	ANU-331	Unionid shell	J. Bowler	6, 10
20	Lake Mungo 5	NSW	Lakeside lunette, shell midden	30,780 ± 520	ANU-680	Charcoal	M. Barbetti	6
20	Lake Mungo 1	NSW	Lakeside lunette, human cremation	24,020 ± 1480 27,160 ± 900	ANU-372a ANU-372b	Charcoal Unionid shell	H. Allen	6
21	Lake Tandou	NSW	Lakeside lunette dune; shell midden	25,500 ± 1,000	ANU 618b 375b	Bone 'collagen' and charcoal	J. Bowler et al	6, 10, 16
22	Lake Victoria	NSW	Lakeside lunette dune; oven/hearth	12,350 ± 170	ANU-703	Charcoal	H. Allen	11
23	Lake Menindee	NSW	Lakeside lunette dune; charcoal and hearth?	18,200 ± 800	Gak-2514	Charcoal	E. Gill	11
24	Lake Yantara	NSW	Lakeside lunette dune; hearth	26,300 ± 1,500 18,800 ± 800	LJ-204 Gak-335	Charcoal Charcoal	R. Tedford N. B. Tindale	4, 5, 6
25	Seton Site Kangaroo Island	SA	Limestone aeolianite rock shelter	26,200 ± 1,100	Gak-2121	Charcoal	G. H. Dury T. Langford-Smith R. Lampert	6
26	Koonalda Cave	SA	Limestone sink hole	>10,940 ± 160 (top of deposit)	ANU-925	Charcoal		12
27	Puntutjarpa	WA	Rock shelter	21,900 ± 540 19,400 ± 450 23,700 ± 850	ANU-245 ANU-148 ANU-244	Charcoal Charcoal Charcoal	R. V. S. Wright and A. Gallus	4, 5, 6, 8, 13
28	Devil's Lair	WA	Limestone Cave	10,170 ± 230 24,600 ± 800	SUA-31	Charcoal	R. Gould C. Dortch and D. Merrilees	15 14

Abbreviations of states: TPNG, Territory of Papua and New Guinea; NT, Northern Territory; Q, Queensland; NSW, New South Wales; T, Tasmania; V, Victoria; SA, South Australia; WA, Western Australia.

which is not yet forthcoming. Either there were two populations—an ancient archaic one being added to or partially replaced by a modern one, which entered the continent some time before 25,000 yr ago—or the founding population itself showed marked polymorphism, perhaps due to hybridisation in the region of embarkation¹⁸. The first solution, which seems the most likely at present, also implies that a great slab of Australia's prehistory still awaits discovery.

Technology

Where they are large enough to be diagnostic, the stone tool assemblages from Pleistocene levels of the sites in Table 1 belong to a single pan-continental technological tradition for which the name 'Australian core-tool and scraper tradition' has been suggested¹⁶. These industries are characterised both by their style of retouch and by the tool types themselves. Most implements are scrapers made from cores or thick flakes and, characteristically, they have steep, step-flaked edges with maximum edge angles approaching ninety degrees. Tools include large domed 'horse-hoof' core-scrapers (Fig. 2 *c, d* and *e*), a variety of steep-edge scrapers (Fig. 2 *f* and *g*) and notched scrapers (Fig. 2 *h*). The robust tough edges of these tools, together with microscopic evidence of use wear and ethnographic analogies, suggests strongly that they were used as hand-held scraper planes for working wood, the notched and concave ones being spokeshaves for de-barking and smoothing shafts. A second group consists of convex-edged scraper-knives and small round-edged scrapers including 'thumbnail' types (Fig. 2 *i*) with delicate fluted retouch and sharp edge angles. In some sites, bipolar cores provided small sharp flakes for cutting (refs. 14, 19, and personal communication from J. Kamminga).

These were tools to make tools; the main extractive ones²¹, according to the ethnographic evidence, were almost certainly wooden spears and digging sticks, together with a variety of basket work and nets, for which no direct evidence has yet survived from a Pleistocene context.

In spite of the paucity of detailed studies, some broad stylistic provinces are apparent within this tradition, implying the maintenance of populations living in regional groups and transmitting their own cultural idiosyncrasies over periods which can be measured in terms of thousands or even tens of thousands of years^{7,11,17,24}.

In two sites on the edge of the Arnhem Land Plateau (Table 1; 5 and 6), White excavated several edge-ground and grooved axe heads of diorite (Fig. 2 *a*), from levels dating to just over 20,000 BP making them the oldest of their class in the world^{23,24}. These were found with, for example, typical steep-edged scrapers and similar associations have come from levels 10,000 yr old at Ngarradj Warde Djokeng in Arnhem Land, the Laura rockshelter in Cape York, and Kaviavana in the New Guinea highlands (refs 3, 22, 23 and personal communication from J. Kamminga), showing that right across tropical Greater Australia at least, ground and hafted axes were an integral part of the Pleistocene tool kit. In the New Guinea highlands, functionally analogous tools are the distinctive waisted blades (Fig. 2 *b*), which make their first appearance together with flaked axe adzes in the 26,000 yr old site of Kosiipe, and are persistent elements in later assemblages in the same region down to recent times^{2,3,23}. Another type of hafted tool—the mounted flaked adze used until modern times in central Australia—may also have a Pleistocene antiquity. A continuous sequence of these types goes back to 10,000 BP at Puntutjarpa in the western desert¹⁷, and further corroboration now comes from Devil's Lair in the far south west, with examples dating to 12,000 BP. Flakes with marks of gum on them, presumably for hafting or holding, have also been dated back to 14,000 and 25,000 BP at this site¹⁴.

In most of the old sites so far excavated, only the lithic component of the technology has survived, but slowly other aspects are being discovered. Bone tools consisting of stout, ground and polished points usually made from macropod fibulae have been found at several sites including Devil's Lair¹⁴ where they go back to 20,000 yr, Clogg's Cave in south-east Victoria at 12,000 yr (personal communication from J. Flood), Kaviavana, New Guinea²⁵ at 10,000 yr and in four Tasmanian sites, where dozens of points and spatulae have been excavated

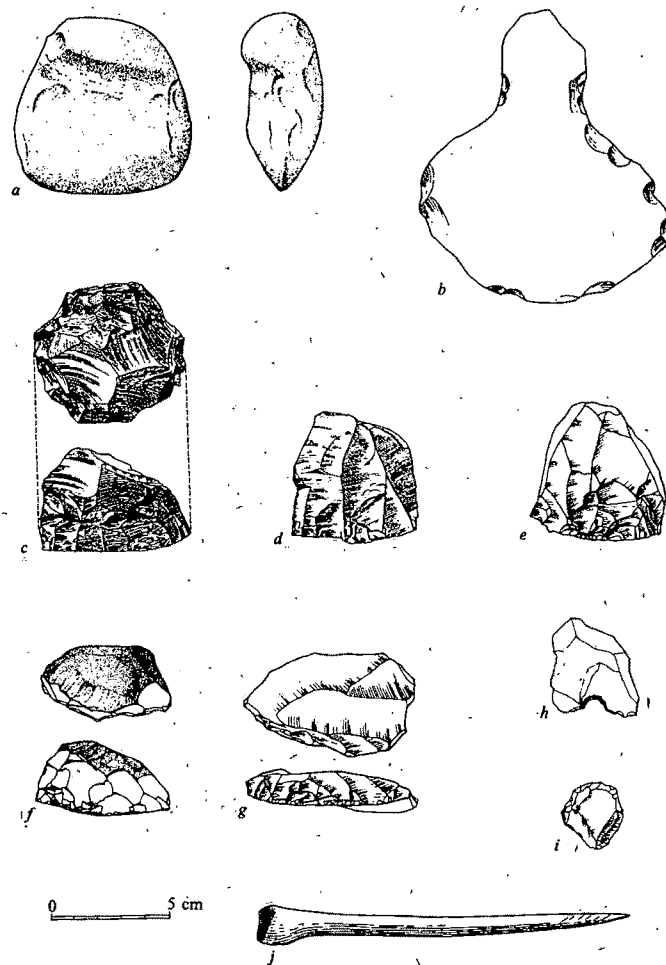


Fig. 2 Some implements of the 'Australian core-tool and scraper tradition'. *a*, Malangangerr, NT (C. White); *b*, Kosiipe, TPNG (J. P. White); *c*, Niobe (Nombe), TPNG (J. P. White); *d*, Kenniff Cave, Q (D. J. Mulvaney); *e*, Lake Mungo, NSW (H. Allen and R. Jones); *f*, Rocky Cape, S; *g*, Lake Mungo, NSW (H. Allen and R. Jones); *h*, Rocky Cape, S; *i*, Burrill Cave, NSW (R. Lampert); and *j*, Devil's Lair, WA (C. Dortch and D. Merrilees).

from levels dated variously from 8,000 up to about 4,000 BP, when they totally disappear from the technology^{4,24}. Their highly distinctive polished use wear, together with ethnographic observations on identical tools, suggests a function as awls and reamers in the manufacture of skin cloaks, such as were used in modern times in south-eastern Australia⁵.

The Australian core-tool and scraper tradition persisted from the earliest sites at 30,000 BP, down to Mid Recent times about 5 or 6,000 BP, when a series of new influences, probably derived from outside Australia became apparent. New Guinea prehistory diverged sharply from that of its mother continent with the introduction of a horticultural economy^{3,23,25}, but the stone tools there still showed remarkable persistence²⁵. In Australia, a range of small tools, such as backed microliths and points were added onto the old technology^{5,17}, and the dingo also entered the continent at this time. Tasmania, isolated for

12,000 yr by the postglacial rising sea, is a special case, since the new influences never reached it. Here a tiny universe of 4,000 hunters survived as direct inheritors of the culture of late Pleistocene Australia until they were destroyed in one generation by civilised man early last century.

Economic Adaptations

Fig. 1 shows that by at least 20,000 BP man was occupying almost all of the principal ecological zones of Greater Australia. During the period under review, the last ice age waxed and waned and caused environmental changes in the highland zones, the continental shelves and the lakes and streams on the edge of the arid zone^{4,10,16}. Yet no matter how much this affected local regions, the basic shape of Australian geography must have been similar to the present day with a large desert core, with its great swirl of continental dunes (Fig. 1), a tropical monsoonal environment to the north, and a cool temperature zone to the south. The arrival of man with fires and hunting pressure had an immense ecological impact, and there is accumulating evidence that man was partially or decisively responsible for the rapid extinction of a large number of 'giant' marsupial and other animals, the principal episode occurring a geologically short time before 30,000 BP. The initial colonisation would have been a period of imbalance and experiment, but by at least 25,000 BP, the distinctive Australian economic system was already in train in some places.

At Mungo, people camped along the sandy beaches bordering the lakes, fishing for golden perch and Murray cod, and gathering freshwater mussels, the shells of which they discarded on midden heaps. From the back scrubs, they collected emu eggs and hunted a wide range of small marsupials including bandicoots and rat kangaroos and cooked their food in earth ovens made by pre-heating lumps of clay^{6,11,16}. In the dry Mungo region, concave sandstone grinding dishes, used for grinding grass seeds into flour, go back from ethnographic times to 15,000 BP; and basal millstones have been found at 18,000 BP in the tropics of Arnhem Land and at 12,000 BP in the rugged hills of south-east Queensland (refs 5, 22 and personal communication from J. Kamminga) implying that a wide variety of seeds and other vegetable foods were part of the diet of late Pleistocene Australians. At the very point in time that the sea reached its present coastline 8,000 BP, the inhabitants of north Tasmania were hunting seals, fishing and diving for shell fish^{4,24}.

There is no reason to think that this coastal economy was a sudden invention conveniently timed to coincide with the end of the Pleistocene, rather the older evidence has been drowned by the rising waters of the Flandrian transgression. This picture of a broadly based foraging pattern extending back from ethnographic times to at least 20,000 BP, has many implications for the study of economic processes in advanced hunting societies. There were no great 'post Pleistocene adaptations'; they had been made a long time before.

The Soul and the Intellect

The young woman at Lake Mungo was cremated and then the calcined bones were smashed and gathered together into a small pit^{10,16,18}. Identical procedures were recorded in Tasmania and the south-east coast of Australia during the last century²⁶, and a continuity for the practice is implied not only by this distribution on both sides of Bass Strait, but also by archaeological finds of cremation pits in Tasmania at 2,000 and the mainland at 10,000 and 12,000 BP^{9,26,27}. A second

Pleistocene burial custom was inhumation, the corpse sometimes being accompanied by grave goods such as stone tools, ochre, shells and animal teeth^{9,27}. The large Lake Nitchie man, buried about 7,000 BP had with him a magnificent necklace consisting of 178 pierced teeth of Tasmanian devils (*Sarcophilus harrisii*), now extinct on the mainland²⁰. Compound burial procedures such as are nowadays practised in northern Australia and perhaps associated with other cultural influences just noted²⁷, seem to have been introduced to the continent in Mid Recent times.

Man left marks of his artistic expression probably as far back as 20,000 BP in the dark subterranean passages of Koonalda^{13,28}, and it is probable that the tradition of rock engravings featuring geometric designs and animal tracks also has a great antiquity²⁸.

When the Upper Palaeolithic sites of Western Europe were first discovered one hundred years ago, it was to the Australian Aborigines that scholars looked for guidance in interpreting their finds. Now, the prehistory of these same Aborigines may mean that decisive innovations in man's cultural development were made on a far broader geographical front than had ever previously been conceived^{8,29,30}.

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Prospects of Astronomy in Australia

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In the first account Dr Bolton, of the CSIRO Division of Radiophysics, Sydney, deals chiefly with radio and solar work. In the second Dr Cannon, formerly a research fellow at Mount Stromlo and now with the United Kingdom 48-inch Schmidt Telescope Unit, highlights the situation in optical astronomy and explains why astronomical research in the Southern Hemisphere is so important.

FOR perhaps ten years after the Second World War, Australia and the United Kingdom shared most of the basic discoveries in radio astronomy. These discoveries have extended the distance horizon of the Universe by an order of magnitude and revealed previously unsuspected sources of energy generation in celestial objects which parallel that of the nuclear energy generated in stars. In many cases, however, the concluding stages of investigations depended on optical astronomers in the United States. It is perhaps fitting that the two countries which independently pioneered the radio field should be partners in a powerful optical instrument, the Anglo-Australian 150-inch telescope at Siding Spring Mountain, New South Wales, for exploration of the relatively unknown southern skies.

Both in Australia and in the United Kingdom the early effort in radio astronomy was made by groups of scientists who had participated in wartime radar development. In Australia the work was concentrated in the Division of Radiophysics of the CSIRO under the leadership of E. G. Bowen and the late J. L. Pawsey. Following Pawsey's initial detection of radio emission from active sunspots, four groups led by J. P. Wild, W. N. Christiansen, B. Y. Mills and myself influenced the direction taken by research at the time; and this in turn led to the present major facilities. Wild, with his dynamic spectrographs, was able to classify and interpret the active phenomena in the Sun's corona—investigations which culminated in the building of Culgoora Observatory. Christiansen with his early grating interferometers, using Earth-rotation synthesis, provided the first high resolution pictures of the Sun at decimetre wavelengths and demonstrated the equatorial limb-brightening. Further developments of this type of instrument led to the Fleurs synthesis telescope, intended for high resolution studies of galactic and extragalactic sources. Mills's investigations showed that radio sources could be divided into two classes, galactic and extragalactic. He was the first to link two aeriels by radio in the study of the angular sizes of radio sources and was the inventor of the Mills-Cross aerial. The Molonglo Cross is now the most powerful instrument in the Southern Hemisphere for radio source surveys. My own group discovered and identified the sources coincident with the Crab nebula and two external galaxies, M87 and NGC5128. The importance of work on radio sources and later the 21 cm hydrogen line led to the building of the Parkes telescope. Both the new optical facilities at Siding Spring (see accompanying account) will greatly assist the extragalactic research at Parkes and Molonglo.

Mainly Solar

In a short article it is impossible to give more than the briefest description of Australian astronomical facilities and their re-

search work. I shall deal chiefly, but not exclusively, with radio and solar astronomy. Most of the major installations are in New South Wales and all but one of these lie on the 'astronomical meridian' 100–200 miles inland from the coast and the dividing range. It is these facilities that most astronomical tourists to Australia visit.

At the northern end of the 'meridian' is Narrabri Observatory, which is operated by the Chatterton Astronomy Department of Sydney University. This is the site of Hanbury Brown's Stellar Intensity Interferometer with its two mosaic mirrors which can be moved on flat cars on a circular rail track 600 foot in diameter. Observations on early-type stars brighter than 2.5 mag for which the instrument was built were essentially completed a year ago. Angular diameters have been measured for thirty-two stars in the spectral range O5 to F8. Other investigations have been made of close binary stars—for example, all orbital elements and the distance of Spica have been determined. The large reflectors are presently being used to measure the Čerenkov light pulses from the night sky in an attempt to detect high energy γ rays ($\sim 5 \times 10^{11}$ eV) from extraterrestrial sources. It is eventually hoped to replace the present instrument with another, a hundred times more sensitive, for work on fainter stars, particularly the Cepheid variables. A proposal for funding such an instrument has been submitted to the Australian government.

At Culgoora, 15 miles west of Narrabri, the CSIRO Division of Radiophysics operates the world's most advanced solar radio observatory; complementary optical facilities are operated by the CSIRO Division of Physics. There is a small flare patrol telescope and two larger optical instruments. One is a 30-cm refractor designed for photography at high resolution (<1 arc s) in either white light or H α . The other is the 'cinemagnetograph', which provides maps of the solar magnetic field with a spatial resolution of 3 arc s. One of the interesting recent discoveries is of Alfvén waves which flow outwards through the umbra and penumbra of a sunspot.

The radio instruments at Culgoora are the dynamic spectrograph and the radioheliograph. The former records the dynamic spectrum of solar disturbances over the frequency range 8 to 8,000 MHz and provides the basic classification of such disturbances. The radioheliograph provides high resolution pictures of the Sun in both left-hand and right-hand circular polarisation at intervals of 1 s at any one of three frequencies. The heliograph consists of ninety-six parabolic reflectors round the circumference of a circle 3 km in diameter. Signals from the individual aeriels are combined to provide forty-eight pencil beams in a north-south line which is step-scanned east-west through sixty positions. At 80 MHz, the initial frequency of the installation, the resulting field of $2^\circ \times 1.6^\circ$ is covered by a matrix of points with a separation of 2.1 arc min; the scanning

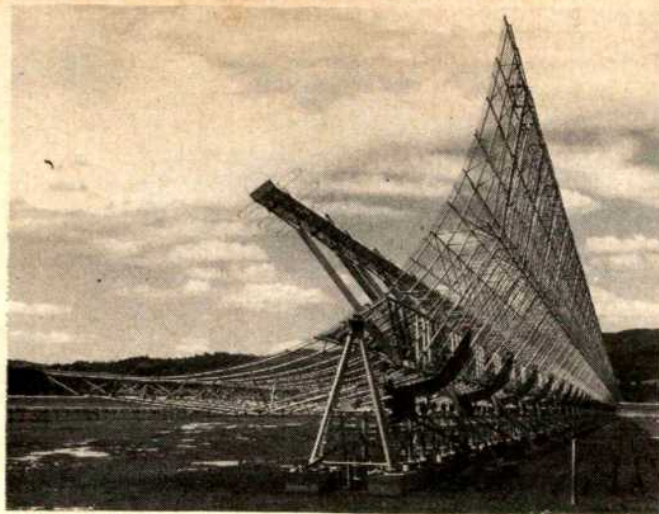


Fig. 1 The east-west arm of the Molonglo radio telescope—operated by the University of Sydney. Overall length is 1 mile. The north-south arm can be seen faintly in the background.

beams have a half-power beamwidth of 3.8 arc min. The same array used at 160 MHz give half the field size and twice the resolution. A second set of forty-eight aeriels has recently been added to provide lower resolution pictures at a frequency of 43.25 MHz.

Observations with the heliograph have shown the sources of solar bursts to be complex, frequently multiple, and at times causally connected in widely separated regions. The connection between the regions can be electron streams (leading to delays of seconds) or magnetohydrodynamic shock waves (resulting in delays of minutes). Many types of burst appear to be emitted at or near the plasma level; their source positions give information not only on coronal electron densities, but also on density fluctuations which scatter the radiation and so allow its wide-angled escape from the plasma level.

Although most burst sources remain stationary some have been observed to move away from the Sun for several million kilometres beyond the plasma level. The radio emission in these cases must be synchrotron radiation. Occasionally the radio spectra of high energy flare events contain trains of remarkably regular pulsations which the spectral evidence suggests are modulated synchrotron radiation. Radioheliograph observations of two of these events showed that the apparent angular size of the pulsating source required transverse speeds $\sim \frac{1}{2}c$ to explain the observed simultaneity. Since the pulsations seem to be closely linked with high energy proton events a fuller understanding of their origin might provide clues to the acceleration of cosmic rays.

The large collecting area (6,000 m²) and high resolving power of the radioheliograph make it also a powerful instrument for galactic and extragalactic research. Flux densities, positions and angular sizes at 80 MHz have been measured for over 2,500 radio sources. Some work has been done on pulsars and on the interplanetary scintillation of radio sources.

Seventy miles south of Narrabri is Siding Spring Mountain near Coonabarabran. Chosen as a site to replace Mount Stromlo as the Australian National University's major observing station, it is also the site of the SRC 48-inch and the AAT 150-inch telescopes. Australian National University instruments on the mountain are the 40-inch, 24-inch and 18-inch telescopes.

Mainly Radio

One hundred and fifty miles further south, near Parkes, is the main centre for galactic and extragalactic research of the CSIRO Division of Radiophysics. The principal instrument is the 210-foot reflector. This was the brain child of E. G. Bowen, and its research record has certainly repaid him for perseverance in acquiring the instrument—perseverance

which surely equalled that of Hale. The 210-foot telescope is probably one of the most successful research instruments ever built and there has been steady upgrading of its surface and receiving equipment. The telescope is used by Radiophysics staff and researchers from Australian universities and overseas institutions to carry out a wide range of research in the wavelength range of 1.25 cm to 2 m. A 60-foot telescope, movable along east-west or north-south rail tracks, can be used alone or as an interferometer with the 210-foot telescope at 21 cm.

The well known Parkes catalogue of radio sources at 408 MHz is being replaced by a much more extensive catalogue at 2,700 MHz and identification work is being carried out in cooperation with Mount Stromlo Observatory. With its facility for simultaneous observation at many different wavelengths the telescope has been used extensively for precise determination of pulsar parameters such as their periods, dispersion measures and polarisation. Most of the pulsars studied were discovered at other observatories, but recently eight new pulsars with very high dispersion measures have been discovered at Parkes using an elaborate anti-dispersion technique developed jointly with the Physics Department of the University of Tasmania.

In the past few years the greatest use of the telescope has been in galactic astronomy, particularly interstellar atomic and molecular spectroscopy. The former includes work on the structure of the interstellar medium through 21 cm line absorption studies, the classification of distant sources as emission nebulae or supernova remnants through observation of recombination lines, and the determination of hydrogen-to-helium ratios in emission nebulae in the Galaxy and the Magellanic Clouds. In the molecular field many sources of OH maser emission have been discovered in the southern Milky Way. A number of new molecules have been discovered as have new transitions of molecules already known in interstellar space. The searches for new molecules and transitions are carried out in cooperation with the Chemistry Department at Monash University, which maintains facilities for laboratory measurements of molecular radiofrequency spectra. Unfortunately the Parkes telescope is not capable of efficient operation below 3 cm where the molecular lines are more numerous; the Radiophysics Division intends to build a 25-m telescope to cover the range from 3 cm to 2 mm when funds become available.

At the southern end of the astronomical meridian are the Molonglo Observatory of Sydney University and the Mount Stromlo Observatory of the Australian National University. An image tube camera at the Cassegrain focus of the Mount Stromlo 74-inch reflector has been used to identify over a hundred southern quasars suggested from radio observations at Parkes and redshifts of many southern radio galaxies have been determined with the image tube spectrograph. Two-colour image tube photography using narrow-band filters has been used at the Siding Spring 40-inch telescope to confirm optically as supernova remnants radio sources in the Magellanic Clouds investigated with the Molonglo Cross. Mount Stromlo observers using the Parkes 60-foot telescope have recently found that the 21 cm 'high-velocity clouds'—long a mystery—probably belong to a stream of gas torn from the Magellanic Clouds in their close passage to our own galaxy. Future studies may provide a fairly precise reconstruction of the dynamics of this encounter.

Probably the most interesting recent work has been on X-ray sources. One of these is 2U0900-40=HD77581, identified at Mount Stromlo. This is a binary and the mass deduced for the unseen companion exceeds the theoretical limit for a neutron star and suggests a 'black hole'. Two other X-ray sources investigated are also candidates for 'black holes'. Supporting evidence is provided by the fact that the X-radiation, presumed to originate from infalling material from the primary, is not pulsed as is the case in other objects where the mass of the secondary is within the neutron star limits.

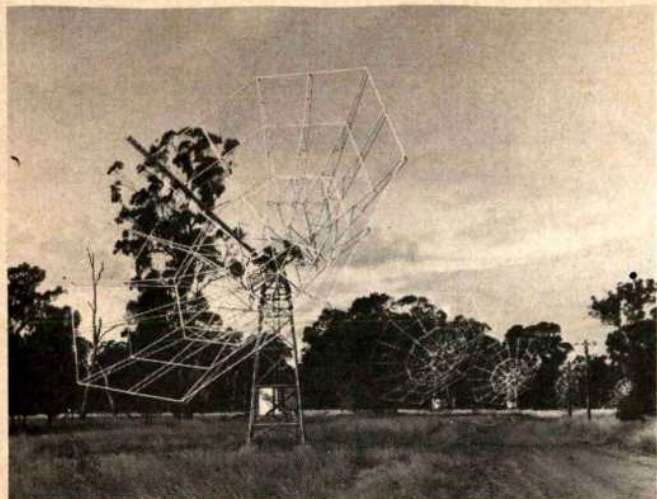


Fig. 2 Some of the ninety-six telescopes that form the Culgoora radioheliograph of the CSIRO.

At Molonglo Observatory there is a Mills Cross with arms 1 mile long operating at 408 MHz with a resolution of 2.8 arc min. A comb of eleven beams along the meridian is produced by simultaneously correlating eleven north-south fan beams with the east-west fan beam. On-line contour maps can be produced on a facsimile recorder. The instrument was designed for a deep survey of the Southern Hemisphere ($\sim 7,000$ sources per steradian). The standard positional accuracy is 10 to 15 arc s, but in special measurements this can be reduced to 2-3 arc s. In addition to the source survey, work at Molonglo includes the identification of supernova remnants in the Magellanic Clouds (discussed previously), spectra and structure of galactic sources—in conjunction with Parkes—and identification of southern quasars and radio galaxies. To aid in the latter a two-coordinate measuring machine has been built. It has been shown that an accuracy of better than 1 arc s can be obtained using the Palomar Sky Survey prints.

The Molonglo telescope, with its very great sensitivity, played an important role in the initial discovery of southern pulsars. At one time over half the known pulsars had been discovered at Molonglo. The results first showed clearly the galactic distribution and the first association of a pulsar with a supernova remnant was suggested.

After completion of the 408 MHz survey, work at Molonglo will probably be phased out and further observations will be made at higher resolution at Fleurs near Sydney. Here the Sydney University School of Electrical Engineering has a rotational synthesis telescope operating at 21 cm wavelength. This is an extension of an instrument built to produce high-resolution pictures of the Sun. A complete map of a region 2° in diameter with a resolution of 40 arc s and a sensitivity of 70 m.f.u. can be obtained in 8 to 12 h. The large number of individual elements provide a complete map in a much shorter time than other synthesis telescopes which use movable elements. With both a north-south and an east-west arm, mapping is possible much closer to the celestial equator than with other instruments. The success of the instrument has been demonstrated by observations of well known objects and routine observations will begin shortly. Projected improvements to the present system are the addition of further elements to double the resolving power and the installation of new r.f. amplifiers to improve the sensitivity five-fold.

Tasmania and Adelaide

Away from the mainland, the island of Tasmania provides an ideal site for low frequency radio astronomy because of both the isolation from terrestrial interference and ionospheric conditions. Grote Reber, one of the American pioneers of

radio astronomy, has worked in Tasmania for many years at very low frequencies. He is currently building a 1-km filled array for work at 1 MHz. The Physics Department at the University of Tasmania has developed techniques for the construction of large broad-band arrays at low frequencies. One array, 760 m in diameter, has been in operation for some time between 2 and 20 MHz and a second, 80 m $\times$ 160 m, for use from 40 to 170 MHz will be complete next year. The latter will be used for pulsar searches and will use the same anti-dispersion technique used in the collaborative programme at Parkes. The low frequency array is in use for studies of the galactic continuum radiation and the interstellar free electron distribution through its absorption effects. Extensive observations of the Jovian decametric radiation are also in progress using a novel video recording system to obtain dynamic spectra of the Jovian bursts with a time resolution of 100μ s and a frequency resolution of 10 kHz.

Some optical observations are being made with a 40 cm telescope but the main effort is directed towards the completion this year of a 100 cm reflector intended for photometric and photoelectric work. The cosmic-ray group at Hobart is continuing a fifteen-year study of cosmic rays from an underground observatory. A 0.1% variation in intensity with sidereal time has been found. An absorption effect has also been found, apparently due to Jupiter, which, to cosmic rays of rigidity in excess of 100 GeV, appears as a solid disk 1.5 to 2° in diameter.

X-ray astronomy, particularly the study of variable sources, is carried out jointly by the University of Tasmania and the University of Adelaide on rockets flown from the Woomera range. The Physics Department at the University of Adelaide also carried out ultraviolet rocket-borne experiments. The absolute solar flux has been determined in the range of 1,400 to 1,700 Å and the minimum solar temperature measured at $4,570 \pm 50$ K. The lunar albedo has been found to drop sharply in the ultraviolet to 0.7% at 2,400 Å and 0.3% at 1,216 Å.

Radar investigations of meteors, begun in Adelaide in 1950, are continuing, with the principal interest in atmospheric investigations. Studies of the solar wind through interplanetary scintillation of compact radio sources are being made at 112 and 236 MHz with aerials at Buckland Park near Adelaide and sites 150 miles north-east and north-west. The aerial at Buckland Park consists of four 200 m corner reflectors with two such reflectors at the outstations. Also at Buckland Park is an array of 178 dipoles on a circle 1 km in diameter. This is at present used for ionospheric sounding at 2 MHz and 6 MHz but it will be used in conjunction with an ultrasonic image-forming system for low frequency radio astronomy near the next sunspot minimum. Finally the radio pulses from cosmic-ray air showers have been found to have an unexpectedly high signal-to-noise ratio near 100 kHz leading to the possibility of the construction of an extensive array of 100 kHz detectors for the discovery of ultrahigh energy ($>10^{19}$ eV) cosmic-ray primaries.

Important Role

So much for the major facilities. This account would not be complete, however, without a reference to the State Government Observatory at Sydney, founded in 1856. This observatory and the one at Perth are the two oldest in Australia. Sydney Observatory played an important though little recognised part in the early stages of radio astronomy in Sydney. It provided the first contact for the radiophysicists with the then conventional astronomy. Its director, Harley Wood, and C. W. Allen at Mount Stromlo Observatory were two people who, for the time, showed a surprising faith in our observations of 'cosmic noise' and 'solar noise' and were always available for consultation. To end on a personal and somewhat nostalgic note, it is twenty-five years ago, this month, that I telephoned Harley Wood and said, "I think that I have identified one of my radio sources. What can you tell me about the Crab nebula?" What, indeed!

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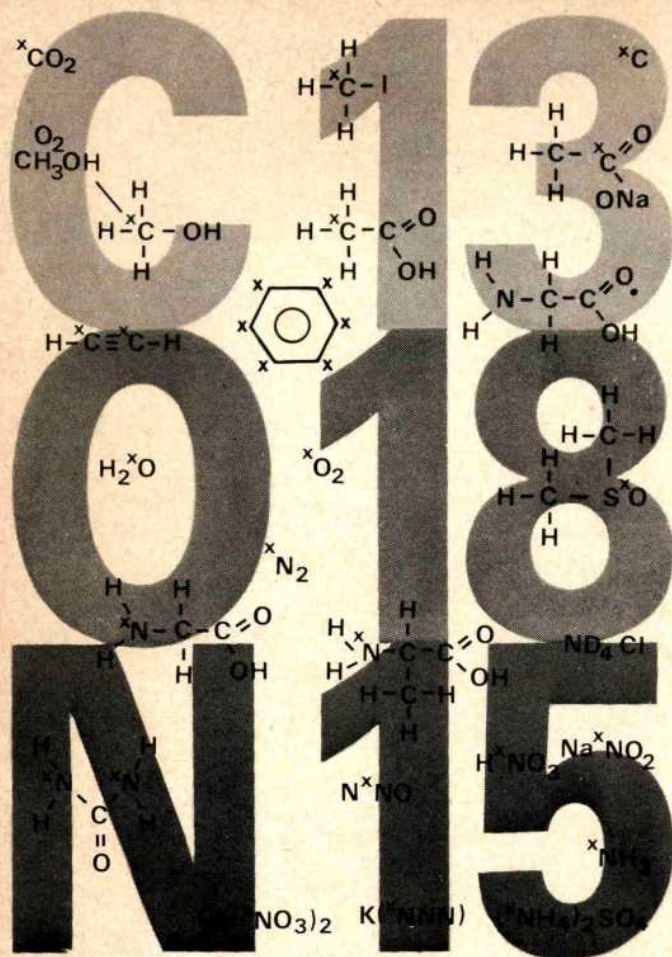
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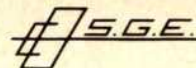
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R. D. CANNON

UK 48-inch Schmidt Telescope Unit, Blackford Hill, Edinburgh EH9 3HJ

AUSTRALASIAN astronomy is of course predominantly Australian astronomy, which today occupies a leading position in the world. This is partly due to a fortunate combination of circumstances: geographical location, giving access to the southern skies which happen to be more important than the northern skies in many fields of research, a good climate, good sites relatively free from man-made interference and an advanced technology. Astronomy is not, however, a young subject in Australia. Over a century ago the Great Melbourne Telescope, with a 48-inch speculum mirror, was one of the world's largest. Initially rather unsuccessful, a much modified version of this telescope containing at least some of the original components is still in regular use on Mount Stromlo. By the turn of this century there were three major government observatories in Australia, at Sydney, Melbourne and Perth, and all three participated for several decades in the international programme to produce the Astrographic Catalogue and Charts covering the entire sky, using standard 13-inch refractor telescopes.

Sydney and Perth Observatories are both active today, mainly in various aspects of positional astronomy, but Melbourne Observatory was closed in 1944 and much of its equipment and library were moved to the then Commonwealth Observatory at Mount Stromlo near Canberra. The latter grew to become Australia's major optical observatory, and is now part of the Research School of Physical Sciences at the Australian National University (ANU). Its pre-eminence in optical astronomy is now passing to Siding Spring, a mountain in the Warrumbungles near Coonabarabran, some 400 miles north of Canberra. Siding Spring Observatory started almost 10 years ago as a field station of Mount Stromlo when the city lights of a rapidly expanding Canberra began to interfere seriously with astronomy. It is now also the site of the United Kingdom 48-inch Schmidt Telescope, and of the nearly completed 150-inch Anglo-Australian Telescope (AAT). Although it is not one observatory administratively, it is to be hoped that there will be close collaboration between the different groups of astronomers on Siding Spring Mountain.

In addition to these conventional observatories, there are two highly specialised optical installations in Australia. These are the Narrabri Stellar Intensity Interferometer, used primarily for the measurement of star diameters, and the Culgoora Solar Observatory of the CSIRO (see accompanying account).

Why Southern Astronomy?

There are several very good reasons why astronomy in the Southern Hemisphere is important. In the first instance, in many fields it is desirable to have complete surveys covering the whole sky. In the study of the structure and dynamics of our own Galaxy, the overall distribution and motions of special types of objects such as star clusters, different kinds of variable stars, pulsars, HII regions and neutral hydrogen, are needed. In cosmological studies, it is very important to know whether or not quasars, radio galaxies and clusters of galaxies are uniformly distributed over the sky and whether or not their velocities are isotropically distributed. For most of these purposes the task is simply to extend northern programmes and catalogues to the south, although in many cases the southern data are now better and more uniform than the northern.

The more exciting projects are those involving specifically southern objects, and it happens by chance that, for many purposes, the Southern Hemisphere is the more important. First and foremost is the fact that the centre of our own Galaxy is situated at -29° declination. Thus, although it is accessible from the major observatories in the southern United States, it is always low on the horizon and only observable for short

periods; by contrast it passes almost through the zenith for Australian observers, and can be followed continuously for many hours with the minimum loss due to atmospheric transparency and turbulence. The galactic centre is, of course, interesting *per se*, particularly at infrared and radio wavelengths which penetrate the intervening matter in the Milky Way, but a secondary consequence is that some classes of objects, for example the globular clusters, are mostly in the Southern Hemisphere.

Globular clusters are important in understanding the history and structure of our Galaxy, as test objects for the theory of stellar evolution, and in the study of stellar dynamics. In addition to the large number of clusters near the galactic centre, the Southern Hemisphere also contains the nearest globular cluster, NGC 6397, and two of the richest and most interesting nearby globulars, ω Centauri and 47 Tucanae. All of these three are south of declination -45° and inaccessible from northern observatories. Perhaps even more important, Australian telescopes have access to the star clusters in the Magellanic Clouds, clusters which seem to be quite different to any in our own Galaxy.

The Magellanic Clouds provide the third and in many ways the best reason for building telescopes in Australia. These Clouds, which appear superficially like detached parts of the Milky Way and which may indeed be satellites of our Galaxy, are much the nearest external galaxies apart from a few dwarf systems more akin to globular clusters, and they lie mainly between declinations -60° and -75° . The study of these two relatively small galaxies may well lead to a basic understanding of how the stars, gas and dust interact in galaxies and of galaxy dynamics and the formation of spiral arm features; by providing

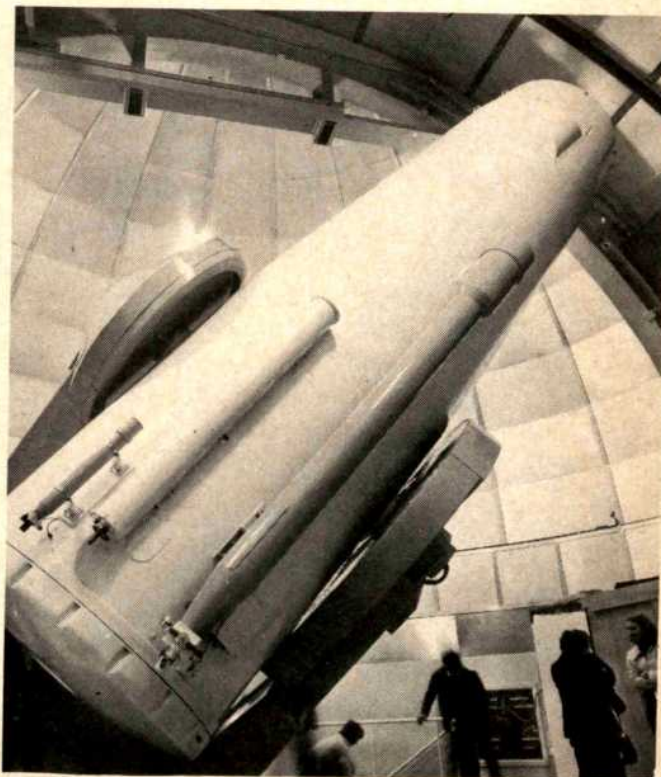


Fig. 1 The United Kingdom 48-inch Schmidt telescope.



Fig. 2 Reproduction of a photograph taken with the 48-inch Schmidt telescope of the United Kingdom Science Research Council, showing the Small Magellanic Cloud.

large samples of all types of objects at almost the same distance, they can also be used to calibrate various distance indicators, as they were for example early this century in setting up the fundamental Cepheid period-luminosity relation.

Astronomy at the ANU

Having outlined some of the reasons why astronomy is important in Australia, I shall describe the work of some of the Australian observatories. The staff at Mount Stromlo and Siding Spring Observatories includes about two dozen research astronomers, approximately equally divided between permanent and short term appointments. There is thus a steady turnover of staff, and a constantly shifting emphasis in the research; there is no single overriding theme in the topics studied. The Mount Stromlo 74-inch is still, with a sister instrument at Pretoria in South Africa, the largest operational telescope in the Southern Hemisphere, and as such is used for a great range of observations; it has instrumentation at three foci: Newtonian, Cassegrain and Coudé. Present projects include high dispersion spectroscopy of bright stars to look for chemical composition anomalies; low dispersion spectroscopy of galaxies to add to the cosmological data on northern galaxies; observations to identify and measure the redshifts of quasars and radio galaxies; the measurement of internal structure and velocities in the nearer galaxies and star clusters; and faint broad-band photometry of star clusters in the Magellanic Clouds and our own Galaxy. The old 50-inch telescope has been extensively used with a photo-electric scanner to determine stellar continuum energy distributions, and a new thirty-three-channel spectrophotometer is now in use on the 74-inch. Other new equipment will permit work in the infrared out to 20 μm on any of several telescopes, including the recently renovated Reynolds 30-inch reflector. There are three ANU telescopes on Siding Spring Mountain, comprising 40- and 16-inch conventional reflectors and a 24-inch reflector with a rotating tube specially designed for polarisation measurements. All three telescopes are used primarily for broad, intermediate and narrow wave-band photoelectric measurements of large sam-

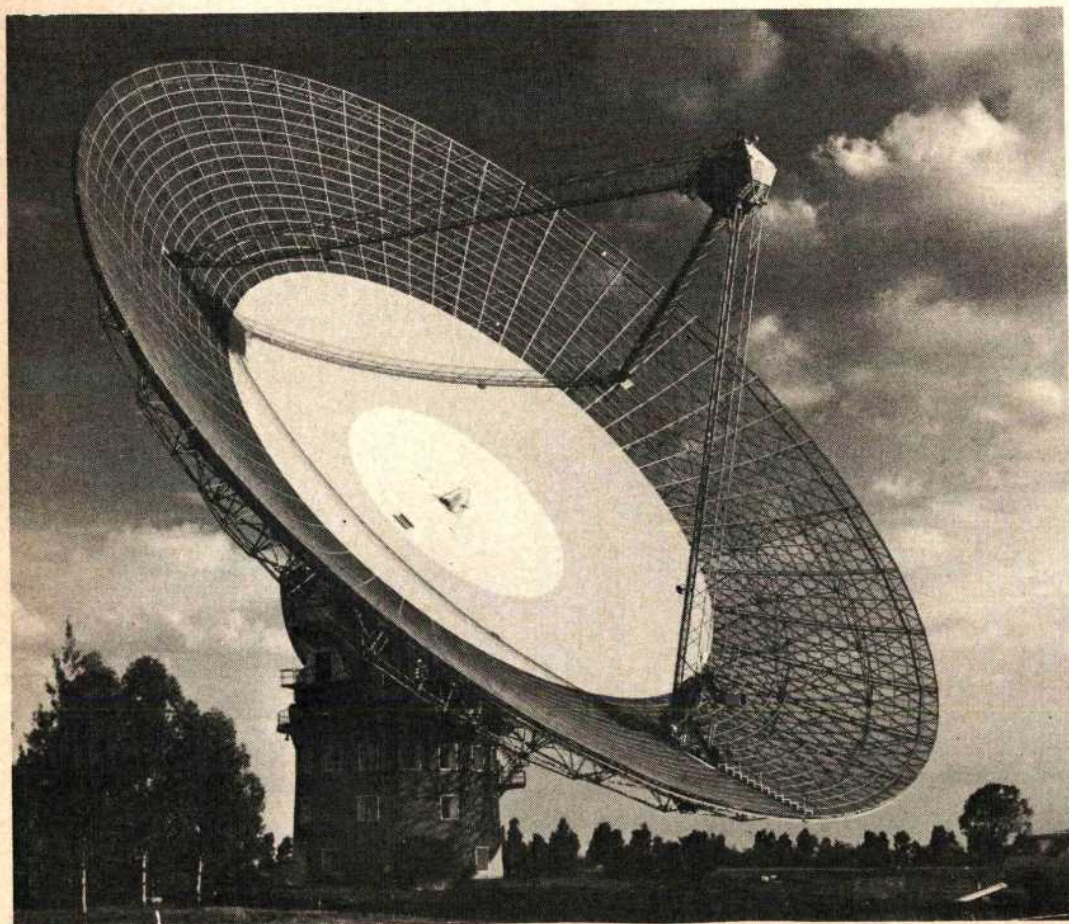


Fig. 3 The 64-m (210-foot) radio telescope at the CSIRO Parkes Observatory, a vital complement to the new optical facilities at Siding Spring.

ples of stars, mainly directed towards elucidating the structure and dynamics of our own Galaxy and some aspects of stellar evolution.

Other Australasian Astronomy

New Zealand has a long tradition of optical astronomy, and is particularly active in the international programmes to monitor bright variable stars. The principal modern observatory is the Mount John Observatory in South Island, operated jointly by the Universities of Canterbury at Christchurch, Pennsylvania and Florida, whose most important work to date is the recently published Canterbury Sky Atlas made using a 24-inch reflector telescope; this should be a useful adjunct to the forthcoming much deeper, larger scale Schmidt surveys. Mention must also be made of the Carter Observatory in Wellington, which fulfils the usual role of a government observatory.

There is another observatory of note in Australasia, the Bosscha Observatory at Lembang in the Indonesian island of Java. The two main instruments here are a 24-inch double refractor and a 20-inch Schmidt telescope, which are used to observe double stars and for photometry of star clusters.

Future Prospects

In the immediate future, the most exciting prospects are in optical astronomy which may be able to recapture some of the glory which has rightly fallen mainly to Australian radio astronomy in recent years, and which has in fact provided much of the motivation for the new optical instruments. The United Kingdom 48-inch Schmidt telescope, owned and operated by the Science Research Council, has recently come into operation on Siding Spring Mountain. It is a specialised instrument, designed only for wide-angle direct photography of the sky, or at a later stage for very low dispersion spectroscopy using an objective prism. It was built primarily to extend the National Geographic Society-Palomar Observatory Sky Survey to the south, and is very similar to the Palomar 48-inch Schmidt; the survey will be done in collaboration with the European Southern Observatory's new 1-m Schmidt at La Silla in Chile.

Important uses of this survey will be the completion of northern catalogues of objects like peculiar galaxies and clusters of galaxies, the identification of radio and X-ray sources, and studies of the distribution of stars and galaxies over the sky. In many fields it will act as an adjunct to the 150-inch AAT, providing source lists of interesting objects for further study.

The 150-inch Anglo-Australian Telescope, with four times the light grasp of the largest telescopes operational at present in the Southern Hemisphere, should make many exciting discoveries; it may well be the first of the new large southern telescopes in regular operation since it is due for completion during 1974. The prime fields of research will probably be the Magellanic Clouds, the centre of our own Galaxy, and interesting peculiar objects such as the radio galaxy Centaurus A (NGC5128). In all these fields, there will have to be close collaboration between optical, radio and the rapidly developing astronomy at other wavelengths.

Recent astronomical research in Australia has opened up so many promising lines of research that the biggest problem at present is to decide on priorities for future instrumentation. For example, three recent major Australian proposals are for a millimetre radio telescope to continue the Parkes/Monash work on interstellar molecules, a new much larger stellar intensity interferometer to extend the Narrabri work to fainter stars, and a 60-inch conventional optical telescope as support for the 150-inch AAT. Although this last is an Australian proposal, there are strong reasons why the UK also should consider providing more supporting telescopes, so that British astronomers can make efficient use of their time while in Australia working on the AAT; the 48-inch Schmidt will only be able to meet part of the need in this respect, and the existing smaller Australian telescopes are already over-subscribed by Mount Stromlo astronomers so that there is unlikely to be much time available on them for visitors. Another obvious gap in existing Australian instrumentation is the lack of a really accurate positional radio telescope. Radio positions are now being determined in the Northern Hemisphere to accuracies of about 1 arc s, but the best southern catalogues give accuracies of only about 6 arc s which is not good enough for unambiguous optical identification of radio sources, particularly of any without obvious optical peculiarities. Furthermore, it seems likely that radio astronomy may in the future provide the basic reference frame for astrometry since it is already capable of higher positional accuracy than traditional optical techniques.

100 Years Ago

THE forthcoming number of Petermann's *Mittheilungen* will contain an interesting article compiled from the Australian papers, giving an account of a three months' journey during August, September, and October of last year into the interior of Australia, by Mr. Ernest Giles, accompanied by Messrs. Carmichael and Robinson. They struck off from the route of the overland telegraph at Chambers's Pillar, about 133° 55' E. long., and 24° 53' S. lat., and journeyed in a north-west direction along Finke Creek, traversing ground which has not hitherto been explored. They passed among long ranges of hills, lying in an east and west direction, and varying in height from a few hundreds to 4,000 ft., though few of the heights are apparently above 1,000 ft. At about the 24th parallel, in 133° N., they came upon multitudes of magnificent fan palms growing along the bed of the creek; they named the place the "Glen of Palms." Their journey in this direction extended to 129° 55' W., and about 23° 10' S., the utter sterility of the region and the want of water compelling them to turn back. It was only during the last few days, however, of their western journey that water became scarce. The most characteristic vegetation throughout was *Spinifex*; *Casuarina* was also of frequent occurrence.

From *Nature*, 8, 94, May 29, 1873.

WELLINGTON N.Z. PHILOSOPHICAL SOCIETY

The President referred to the expected visit of the *Challenger* on a scientific exploration of the Southern Seas, and expressed a hope that it would add largely to our knowledge on this interesting subject. Referring to the great Southern Continent, which is full of interest with its active volcanoes amidst perpetual snows, he stated it was likely that the ensuing year will add greatly to our knowledge of that land, which is only 1,200 miles distant from New Zealand, on whose climate it probably exerts a marked influence. This little known land possesses large supplies of guano, and according to Sir James Ross, has a large and undisturbed whaling ground near it, in which whales of several different species abound. The President criticised Captain Hutcheon's paper on the Glacial period of New Zealand, and confirmed his dissent from the theory of a submergence of the New Zealand area on a grand scale during the post-pliocene or post-glacial period, and stated that unless palaeontological evidence of recent date can be obtained from strata occupying valleys that were eroded during the last extension of the glaciers he must still adhere to his formerly expressed opinion, that the geological period previous to that which may be termed the recent period in New Zealand was characterised by a prolonged though perhaps not excessive elevation; and that especially in the South Island there is in consequence a marked absence of marine drifts and tills. The President commended the study of the subject of our soils, surface drifts, and beach rocks to the members of the Society.

From *Nature*, 9, 173, January 1, 1874.

Relative Motion of Hot Spots in the Mantle

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Reconstruction of the major lithospheric plates 21 and 38 m.y. ago implies that linear island chains and aseismic ridges were not generated by localised sources of volcanism (hot spots) that have been fixed with respect to one another. If the linear volcanic chains are formed over mantle hot spots, the spots move at rates of 0.8 to 2 cm yr⁻¹ with respect to one another.

CAREY¹ suggested that many of the aseismic ridges observed on the ocean floor are manifestations of hot spots in the mantle and assumed, as Dietz and Holden² did later, that these aseismic ridges could be used in reconstructions of continents earlier in the Cainozoic. Wilson^{3,4} further suggested that they were generated as the seafloor moved over localised zones of upwelling that are fixed with respect to one another in the mantle beneath the asthenosphere. Morgan^{5,6} attributed the hot spots to convective plumes rising from the lower mantle. We explore here the assumption that the hot spots are fixed with respect to one another and therefore define a reference frame with respect to which the plates move.

Reconstruction of Plates

One test is to examine the relative positions of the major plates at some time in the past and locate one of them properly over its hot spots. If all the hot spots are fixed with respect to one another, then they should all underlie the linear volcanic chains that they generated. Minster *et al.*⁷ used inversion techniques to obtain a refined version of recent relative plate motions, and made a preliminary test by comparing the trends of linear volcanic chains with those predicted. They found no observable relative motion of the hot spots during the past few million years. Because changes in spreading rates occurred between about 5 and 20 m.y. ago at nearly every major spreading centre in the oceans, their instantaneous velocities are probably not useful for periods earlier than 10 m.y. ago.

The relative positions of pairs of plates at different times earlier in the Cainozoic have been reconstructed in the North Atlantic Ocean⁸, in various parts of the Indian Ocean⁹⁻¹¹, and in the South Pacific¹². Spreading in the

South Atlantic has been relatively constant, so that Le Pichon's¹³ original pole and angular velocity are probably sufficient for our purposes. These studies allow one to interrelate the motions of all the major plates.

We reconstructed the plates to their positions with respect to one another at different times in the Cainozoic. Then, assuming the Hawaiian-Emperor chain to be the expression of the motion of the Pacific Plate over the Hawaiian hot spot, we rotated the Pacific Plate along with the reconstruction of the other plates to their positions with respect to the Hawaiian hot spot. The reasons for constraining the reconstructions to agree with the inferred relative positions of the Pacific over the Hawaiian hot spot are: (1) using other island chains in the Pacific Ocean the pole of relative motion between the Pacific Plate and the hot spots can be well determined; (2) the dating of islands along the chain is more complete than along any other; and (3) there is more complete agreement that the Hawaiian Islands were generated by a hot spot than for most of the other suggested ones. If the other hot spots did not move with respect to the Hawaiian spot, then for each of these reconstructions the linear volcanic chains should overlie the hot spot that generated them.

We considered the hot spots and linear volcanic chains listed in Table 1. These were selected because they are among the more popular ones and they have a balanced geographical distribution. We recognise that there is no unanimity as to what constitutes a well defined hot spot.

We made reconstructions for 21 and 38 m.y. ago. For earlier times, the data are not yet adequate to reconstruct the major plates reliably. For 21 m.y. we used reconstructions to anomaly 6 in the Pacific, South-east Indian and South Atlantic oceans and interpolated between earlier and later reconstructions in the North Atlantic and North-east Indian Ocean. Assuming the age of Midway Island to be 18 m.y.¹⁴, the position of the inferred Hawaiian hot spot with respect to the Hawaiian chain 21 m.y. ago is relatively

Table 1 Hot Spots and Volcanic Chains

Hot spot	Linear volcanic chain	Fig.
Hawaii	Hawaiian Islands	1
Gough Island and Tristan da Cunha	Walvis Ridge and Rio Grande Rise	2
Réunion	Mauritius Plateau and Chagos-Laccadive Ridge	3
Kerguelen	Ninety East Ridge	4
St Paul's and Amsterdam Island	Ninety East Ridge	4
Iceland	Greenland-Iceland and Iceland-Faeroes Ridges	5
Yellowstone	Snake River Basalts	1

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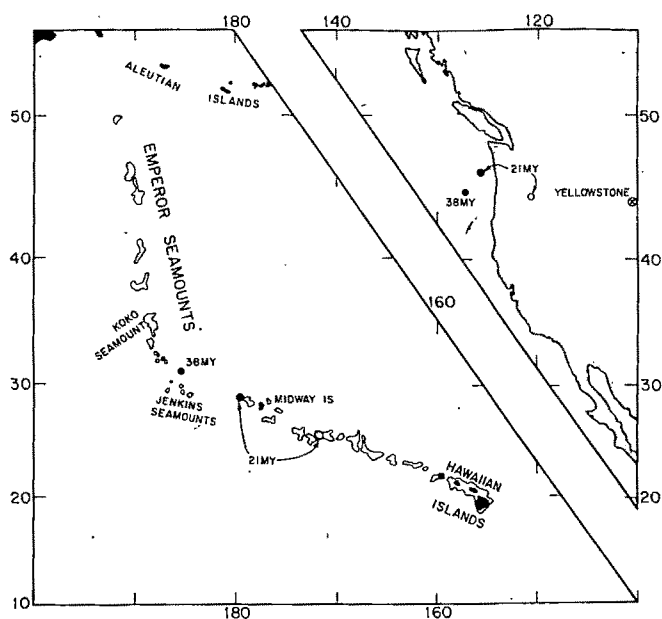


Fig. 1 Left, Hawaiian-Emperor chain and positions of the Hawaiian hot spot at the present and at 21 and 38 m.y. ago. Position at 38 m.y. ago is based on the age of Koko seamount¹⁵. Two estimates for 21 m.y. ago assume: ●, Jackson *et al.*¹⁴ date of Midway or, ○, constant rate of Pacific motion over hot spot. ⊗, Present position of hot spot. Right, calculated position of Yellowstone hot spot with respect to North America at 21 and 38 m.y. ago.

well defined (Fig. 1). Assuming that the hot spots are fixed with respect to each other, the reconstructed positions of the plates at 21 m.y. show that, except for the Ninety East Ridge, the other hot spots do not underlie the aseismic ridges generated by them (Figs 2 to 5). If the 18 m.y. age of Midway approximately dates the passage of the Hawaiian hot spot, that spot cannot be fixed with respect to the others⁷.

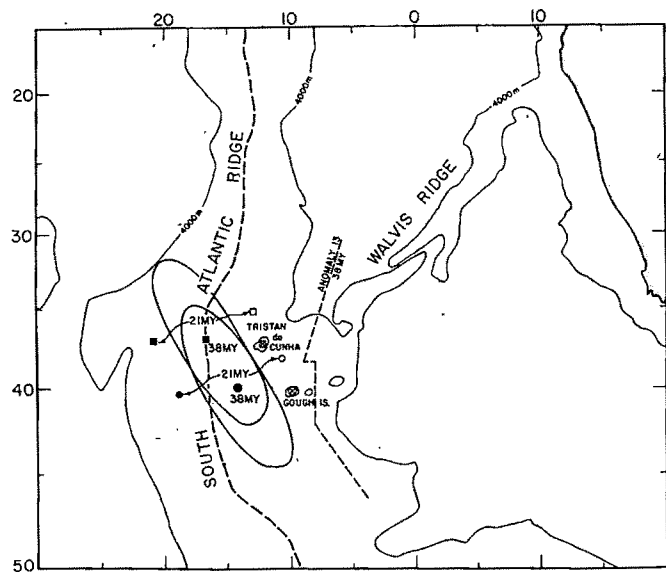


Fig. 2 Relative positions of hot spots under Gough Island and Tristan da Cunha with respect to the African Plate. Symbols as for Fig. 1. Confidence oval surrounds position for 38 m.y. ago. If fixed to the Hawaiian hot spot, the two proposed hot spots should underlie the Walvis Ridge beneath material older than 21 m.y. and 38 m.y. The calculated positions lie beneath material that had not yet been formed at these times. Therefore, at these times, they lay beneath the South American Plate, south of the Rio Grande Rise. They could not have generated these ridges and also been fixed to the Hawaiian hot spot.

In view of the possibility that the Midway age does not date the formation of the island, we decided to explore the possibility that the rate of motion has been constant for 42 m.y. during the entire formation of the Hawaiian chain (Fig. 1). Although the disagreement is less than for the case above (open circles in Figs 2 to 5), the calculated positions of the other hot spots still do not lie under the traces presumed to be generated by them. Because of the various interpolations involved in the 21 m.y. reconstruction, this conclusion is, however, not inescapable.

The reconstructions for 38 m.y. ago provide a more definitive test. Dating of Koko seamount¹⁵ constrains the Hawaiian-Emperor bend to be about 42 m.y. old¹⁶. Anomaly 13, a prominent magnetic anomaly used in the reconstructions of most oceans, was formed approximately 38 m.y. ago. Thus the uncertainties both in the relative positions of the major plates and in the assumed position of the Pacific Plate with respect to the Hawaiian hot spot are likely to be smaller than for other times. The relative

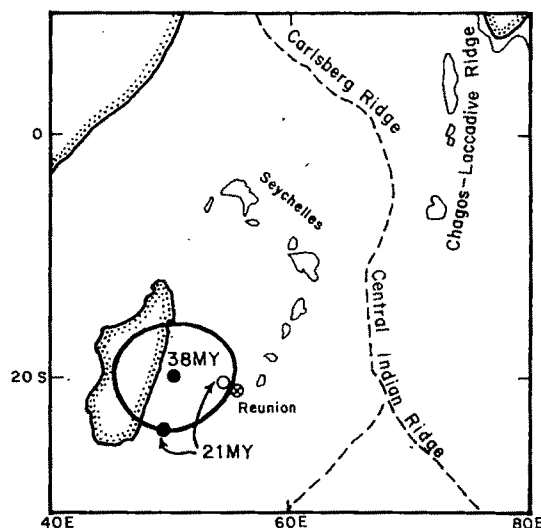


Fig. 3 Relative position of the hot spot under Réunion with respect to the African Plate. Symbols same as Figs 1 and 2. The Mauritian Plateau and the Chagos-Laccadive Ridge were continuous 38 m.y. ago^{9,10}. If this hot spot generated the Mauritian Plateau, and the Chagos-Laccadive Ridge on the Indian Plate, and fixed with respect to the Hawaiian hot spot, it should lie beneath the Mauritian Plateau north-east of Réunion. It does not.

positions of the hot spots and their associated linear island chains at 38 m.y. are shown in Figs 2 to 5. Except for the possibility that a hot spot beneath Kerguelen generated the Ninety East Ridge, the calculated positions of the spots are not coincident with the chains presumed to be generated by them. If the hot spots formed these chains, they have moved 300 to 800 km with respect to the Hawaiian hot spot, that is, at rates of 0.8 to 2 cm yr⁻¹. These rates are comparable with those for relative motions of most of the plates, although they are significantly slower than those in the Pacific.

Uncertainties and Assumptions

The uncertainties in the reconstructions result from two sources: errors in individual reconstructions and validity of the assumptions. Both are difficult to evaluate. One may gain a crude, upper limit for the reconstruction errors in the following manner. The uncertainties in the positions of the poles matter very little except that they are coupled to uncertainties in the angles of rotation. The uncertainties in the angles are not likely to be greater than 1° (see also

2° for the Pacific hot spot rotation). Thus at the equator for each rotation, an error of about 100 km could result. For example, the position of Gough Island with respect to Africa requires four rotations (Africa→India→Antarctica→Pacific→Hawaiian hot spot). The maximum uncertainty would be about 400 km. As Gough Island does in fact lie near the equator of each of the four rotations, this estimate is a reasonable upper limit. The motion of the Iceland hot spot with respect to the North American Plate involves five rotations (North America→Africa→India→Antarctica→Pacific→Hawaiian hot spot). In three of these (the first one and the last two), the pole of rotation is near Iceland. Thus the error in relative position should be considerably less than 500 km.

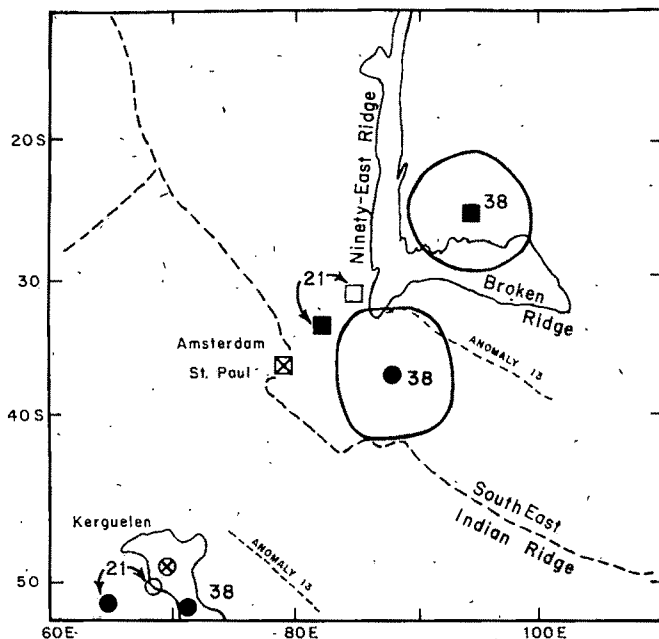


Fig. 4 Relative positions of hot spots beneath St Paul's and Amsterdam Islands with respect to the Ninety East Ridge on the Indian Plate (squares); and of Kerguelen hot spot with respect to the Kerguelen Plateau on the Antarctic Plate (circles) and with respect to the Indian Plate for 38 m.y. ago (closed circle with confidence oval). Symbols as in Figs 1 and 2. If either of these hot spots had generated the Ninety East Ridge and were fixed with respect to the Hawaiian hot spot, it should lie between the Ninety East Ridge and Kerguelen 21 and 38 m.y. ago. If a hot spot exists beneath Kerguelen and generated the Kerguelen Plateau, it should have lain beneath it during the past 38 m.y. The data do not rule out the possibility that a hot spot beneath Kerguelen, fixed with respect to Hawaii, could have generated both of these features. No such feature beneath St Paul's and Amsterdam Islands could have produced the Ninety East Ridge.

Since the above error estimates tend to be excessive, we performed a more realistic calculation. We were not able to treat the uncertainties in a statistically rigorous manner, so we simply estimated the maximum uncertainty in each of the finite rotations and explored the range of possible combinations of them. This procedure allowed determination of ovals describing the largest possible errors in the relative positions of the hot spots with respect to the plates. These ovals are shown in Figs 2 to 5 for the reconstructions for 38 m.y. ago. They show that the relative motion of any given hot spot with respect to the Hawaiian hot spot can be reduced by about a factor of two. Because the uncertainties are not independent, it is not, however, possible to reduce all of the motions this much.

Apart from assuming the Vine-Matthews hypothesis to be correct so that given anomalies on opposite sides of a

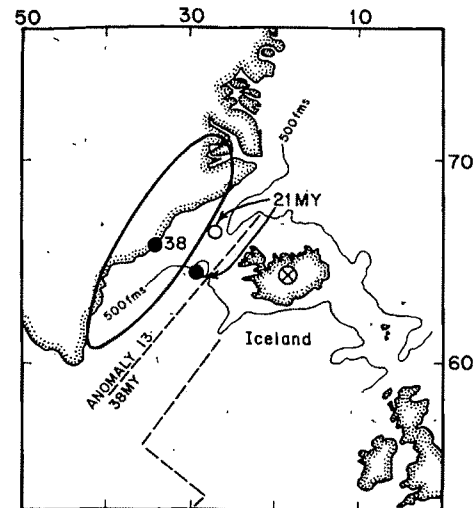


Fig. 5 Relative positions of a hot spot beneath Iceland with respect to the North American Plate. Symbols as in Figs 1 and 2. If the ridges between Greenland and Iceland and between Iceland and Europe were produced by a hot spot beneath Iceland, it would have been centrally located with respect to Greenland and Europe during the past 38 m.y. When fixed with respect to Hawaii, it is found to have underlain the North American Plate during this time, and therefore could not have generated the Iceland-Faeroes Ridge.

spreading centre were formed at the same place, the crucial assumption is that the plates are rigid. There seems to be no reason to doubt this in the oceanic areas. We neglected deformation along the East African Rift, because it is much smaller than the uncertainties discussed above. The possibility of deformation in Antarctica is difficult to eliminate. Motion between East and West Antarctica has occurred since the Jurassic¹⁷⁻¹⁹ and seems to have continued into the Cretaceous¹². The reconstruction of the South-West Pacific Ocean at 38 m.y. does not require younger deformation¹², so we assume that Antarctica has behaved rigidly since then. In any event, if deformation has occurred since 38 m.y. ago in the same sense as earlier, it seems that the resulting relative positions of the hot spots and associated linear chains would differ even more than shown in Figs 2 to 5.

Perhaps the strongest justification for the reconstructions used here comes from the estimated relative position of the Pacific and North American plates, for 38 and 29 m.y. (ref. 20). These reconstructions place the extinct Pacific-Farallon spreading centre a few hundred km west of North America at 38 m.y. ago, and within 200 km of the coast 29 m.y. ago. These calculated positions agree well with those inferred from the magnetic anomalies in the Pacific Plate west of California^{21,22} and their differences are far less than the maximum uncertainties cited above.

We carried out one other check. If there was some unknown deformation within one of the plates or if the reconstruction between one pair of plates was grossly in error, and if the hot spots were fixed, then an additional, arbitrary rotation exists that when added into the sequence of rotations would allow all of the aseismic ridges to overlie their respective hot spots. To carry out such a search rigorously is expensive and tedious. But a manual examination using a globe revealed no such arbitrary rotation. For instance, rotations that caused the Iceland hot spot to lie beneath the Iceland-Faeroes ridge invariably left the Walvis Ridge far north of the hot spot inferred to lie at present beneath Gough Island or Tristan da Cunha.

Implications for Plate Motion

If the hot spots are fixed with respect to each other, what does this imply for plate motions and the origin of linear

volcanic chains? First⁷, it requires that Midway be considerably older than the date given by Jackson *et al.*¹⁴. Second, more than one of the pole positions and finite rotations used here must be grossly in error. Third, there must be a large internal deformation within Antarctica since 38 m.y. ago, in some sense different from that calculated to have occurred earlier in geological time¹². We consider a simpler interpretation to be that the hot spots do not define a fixed reference frame, that the Hawaiian hot spot moves at velocities with respect to the others that are comparable to the velocities of relative plate motions, and that the others also move with respect to one another. Burke *et al.*²³ reached a similar conclusion concerning motions among the various Atlantic hot spots since the Cretaceous, and McElhinny²⁴ concluded that hot spots could not be fixed both with respect to one another and to the spin axis of the Earth. Although relative motion of the hot spots of the magnitude suggested here does not prove that plumes do not exist, it does refute one of the most appealing aspects of the idea: a fixed reference frame with which to describe the motions of the plates; and it removes a strong impetus for placing their origin in the lower mantle.

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Sequence of Events in Plasma Membrane Assembly during the Cell Cycle

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Major components of the plasma membrane double during interphase. Some minor components also double, but others show fluctuations. Decreased expression by immune cytotoxicity of H-2 antigenicity during interphase is explicable in terms of decreased membrane fragility. These results are compatible with a model in which plasma membrane assembly occurs throughout interphase and in which cytokinesis is essentially a physical process.

THE importance of the cell surface in biological processes makes knowledge of the mechanism of its assembly highly

pertinent. At present, for example, it is not known whether the components are synthesised predominantly during mitosis or during interphase. The development¹⁻⁹ of a technique^{10,11} of separating cells by size according to their position in the cell cycle has enabled us to make some initial observations¹² on the assembly of cellular membranes; we found that the protein, as well as some specific enzymes, of nucleus, mitochondria and endoplasmic reticulum doubles during interphase. A procedure for isolating plasma membrane^{13,14} has now enabled us to study the assembly of its components during the cell cycle. An extension of previous observations¹⁵ on the expression of surface antigens provides further support for a model for the assembly of the plasma membrane¹⁶⁻¹⁸.

Ratio of Surface Area to Volume

Like most cultured cells, those used in this study double in volume between G_1 and G_2 (ref. 6). Since they are spherical the surface area increases by a factor of $2^{2/3}$ or approximately 1.6: the extra 0.4 is presumably made up

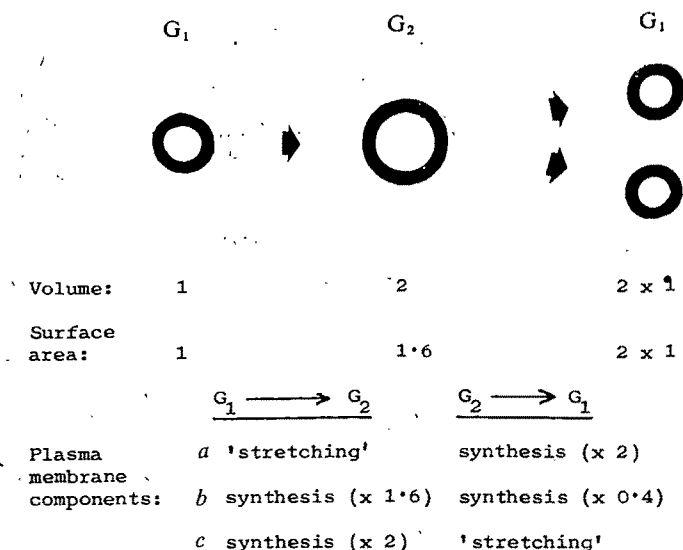


Fig. 1 Models of plasma membrane assembly during the cell cycle.

between G₂ and the next G₁ period, that is during mitosis (Fig. 1). Provided cell shape remains unaltered during growth, the deficit in surface area is approximately 0.4 for other shapes (for example, a flat disk) also. Only when growth is unidirectional, as in bacteria, does the deficit approach zero. By 'stretching' (Fig. 1) we do not wish necessarily to imply a 'ballooning' mechanism. An unfolding of previously-formed convolutions or ruffles¹⁹ is equally possible. Electron microscopic investigations are in progress to elucidate these alternatives.

In order to distinguish between the three possible mechanisms (Fig. 1a-c), we have now measured the content of the components of the plasma membrane, relative to the rest of the cell, during the cell cycle.

Cultured mouse mastocytoma cells (P815Y) and virally-transformed hamster fibroblasts (NIL-2HSV) were exposed to a pulse of ³H-thymidine before separation on a zonal rotor. Cells were allocated to a particular position in the cell cycle on the basis of (1) amount of ³H-thymidine incorporated, that is, ³H-DNA synthesis, (2) content of DNA and (3) cell size (Fig. 2); like P815Y cells²⁰, NIL-2HSV cells have rather long G₁ and S periods and a short G₂ period. Several runs were carried out with each line and cells at particular stages were pooled and disrupted by nitrogen cavitation. Nuclei were removed by centrifugation and the supernatant separated into mitochondria, endoplasmic reticulum and plasma membrane by high speed zonal centrifugation through a sucrose-dextran gradient^{18,14}. NIL-2HSV cells were used for the measurement of some enzymes because P815Y cells contain exceptionally low amounts (for example, 5'-nucleotidase); conversely, P815Y cells were used to measure carbohydrate content because of a more extensive study in progress (M. C. B. S. and C. A. P., unpublished).

Major Components

Figure 3 shows that the yield of plasma membrane protein, in terms of total cellular protein, is constant between G₁ and G₂ and therefore reflects a gradual doubling⁶ in plasma membrane protein during interphase. The possibility that plasma membrane protein includes protein adsorbed from the growth medium has to be borne in mind. Polyacrylamide gel electrophoresis does not reveal major changes in the pattern of plasma membrane proteins between G₁ and G₂. The ratio of plasma membrane phospholipid to protein remains fairly constant (Fig. 3), and therefore phospholipid, like protein, is inserted gradually throughout interphase.

In the case of carbohydrate, there is a slight fluctuation in ratio (Fig. 3), indicating a somewhat greater rate of synthesis and insertion during G₁, followed by a relative decrease, the ratio of carbohydrate:protein being restored in G₂. Measurement of individual sugars shows little variation in content of mannose, galactose or glucose during the cell cycle; fucose seems to be added predominantly in early G₁, glucosamine in late G₁, and sialic acid in late S-G₂. This is compatible with other studies^{21,22} showing that mitotic cells contain relatively more sialic acid than do cells in interphase. Fractionation of cellular carbohydrates into glycolipids, gangliosides and glycoproteins confirms these trends in showing an overall increase of each species during interphase (M. C. B. S. and C. A. P., unpublished).

We may conclude that the bulk of plasma membrane components increases during interphase and that the amount present in G₂ is approximately double that in G₁. In other words mechanism c of Fig. 1 is operative. One cannot, however, entirely dismiss mechanism b on the present evidence alone. Studies with cells actually proceeding through mitosis are currently being carried out to confirm this point. It is clear that mechanism a, suggested by earlier observations on bacteria^{23,24} or on animal cells synchronised by treatment with chemical inhibitors^{25,26}, is unlikely. Discrepancies arising from the use of chemically synchronised cells have frequently been documented (see, for example, ref. 27). Mechanism c is compatible with the observation that the concentration of membrane particles as revealed by freeze-fracture is maximal just before mitosis, after which the concentration drops rapidly to reach a minimum some time in G₁ (ref. 28). Mechanism c is also consistent with the proposition that cytokinesis is essentially a physical, contractile process in animal cells²⁹. It differs in that regard

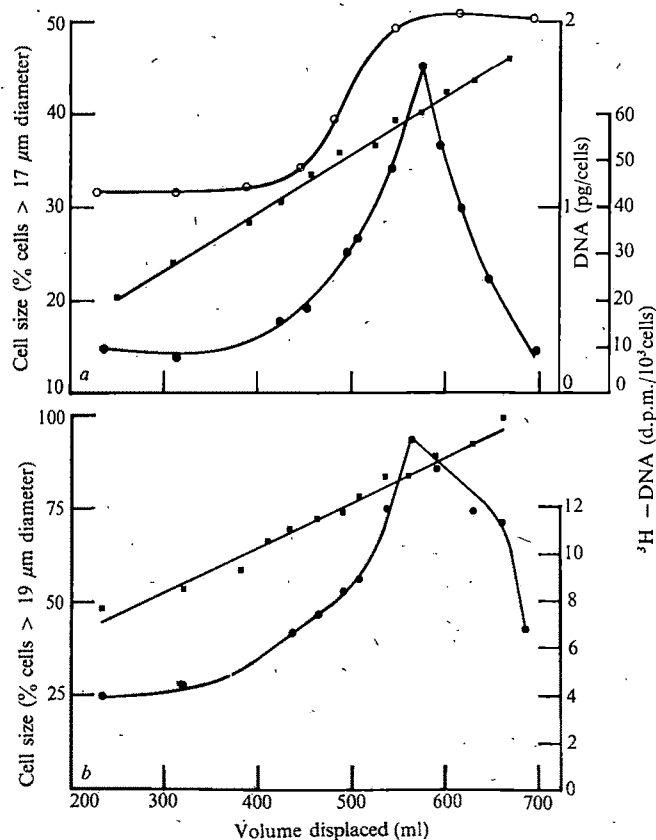


Fig. 2 Separation of cells by size. a, P815Y or, b, NIL-2HSV cells (10^6 – 10^7 ml⁻¹) were exposed to ³H-thymidine (1–2 μCi ml⁻¹) for 30–60 min, washed and separated by low-speed zonal centrifugation⁶. ³H-DNA (●); total DNA (ref. 52) (○); and cell size (ref. 6) (□) were measured.

from mucopeptide wall formation in microbes, in which septal growth is probably accompanied by net synthesis³⁰.

Minor Components

When the activity of an enzyme just doubles during the cell cycle, it is reasonable to assume that the increase reflects a net synthesis of enzyme molecules^{19,31}. This is the case with 5'-nucleotidase (Fig. 4a), though with chemically-synchronised cells a different result has been obtained³². When the activity fluctuates³³, as in the case of Na⁺/K⁺-ATPase (Fig. 4b) or adenylyl cyclase (Fig. 4c), activation or turnover is superimposed on net synthesis. We have not yet distinguished between these two alternatives, but in other systems, turnover (involving temporal separation of synthesis and degradation) has been shown to occur³⁴.

The significance of the increased activity of Na⁺/K⁺-ATPase in late interphase (Fig. 4b) is not clear. It may be related to ionic fluctuations³⁵ which may affect volume and hence density³⁶ or which may control intracellular processes such as DNA synthesis³⁷; alternatively the enzyme may be sensitive to surface changes (see ref. 38) that occur during the cell cycle. In that regard it is interesting to note that the activity of the Na⁺/K⁺-insensitive ATPase behaves like that of 5'-nucleotidase. Fluctuations in a Ca²⁺-activated ATPase have been related to nuclear events during the cell cycle³⁹. The fact that Na⁺/K⁺-ATPase activity is restricted to the plasma membrane at all stages of the cell cycle (Table 1) means that significant amounts of enzyme do not accumulate at the site of synthesis (presumed to be the endoplasmic reticulum). In other words, insertion of components into the plasma membrane appears to follow closely upon synthesis.

The variation in activity of adenylyl cyclase (Fig. 4c) does not agree with results obtained with chemically synchronised cells⁴⁰ in that high activity in mitotic cells is not apparent. Adenylyl cyclase activity assayed in the absence of fluoride shows the same trends as those depicted in Fig. 4c. Our

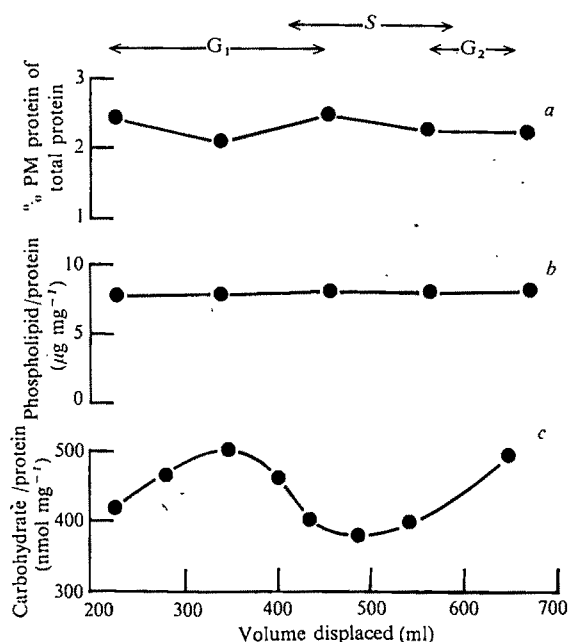


Fig. 3 Content of plasma membrane components during the cell cycle. NIL-2HSV (a and b) or P815Y (c) cells were separated by low-speed zonal centrifugation and pooled fractions disrupted by nitrogen cavitation. Plasma membrane (PM) was isolated by high-speed zonal centrifugation¹³ and the content of, a, protein⁵³, b, phospholipid phosphorus⁵⁴ and, c, carbohydrate (sum of individual sugars separated by gas-liquid chromatography⁵⁵) measured. The periods of the cell cycle, based on Fig. 2, are indicated.

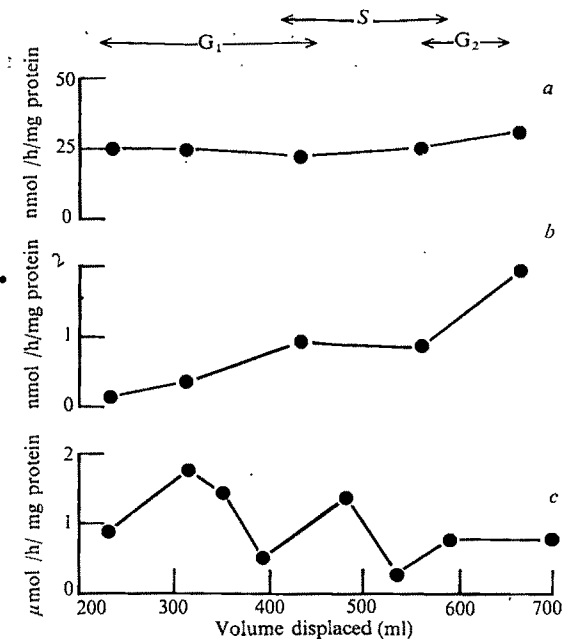


Fig. 4 Activity of plasma membrane enzymes during the cell cycle. NIL-2HSV (a and b) or P815Y (c) cells were separated by low-speed zonal centrifugation and pooled fractions disrupted by nitrogen cavitation (a and b) or by freeze-thawing (c). The activity of, a, 5'-nucleotidase⁵¹ and, b, Na⁺/K⁺-ATPase⁵¹ in plasma membrane isolated by high-speed zonal centrifugation, or of, c, adenylyl cyclase in the presence of 10 mM fluoride⁵⁶ in total cell debris, was measured; in the case of adenylyl cyclase, values are means of two separate determinations. The periods of the cell cycle, based on Fig. 2, are indicated.

results fit better with the observation⁴¹ that the intracellular content of cyclic AMP reaches a peak in G₁, with a second peak before mitosis. A decreased concentration of cyclic AMP in mitosis relative to interphase has also been observed by Burger *et al.*⁴². It is, however, by no means obvious that levels of adenylyl cyclase and cyclic AMP are necessarily related⁴². Moreover in the present experiments, total adenylyl cyclase activity was measured, and independent fluctuations in a nuclear enzyme^{43,44} would complicate the picture. It is therefore premature to speculate on possible roles of adenylyl cyclase in triggering specific events during the cell cycle.

Table 1 Subcellular Distribution of Na⁺/K⁺-ATPase during Cell Cycle

Fraction	% in plasma membrane
1	95
2	92
3	90
4	85
5	90

NIL-2HSV cells were separated by low-speed zonal centrifugation⁶ and five fractions (corresponding to G₁→S→G₂ periods) disrupted by nitrogen cavitation, centrifuged to remove nuclei, and the supernatant separated into mitochondria, endoplasmic reticulum and plasma membrane by high-speed zonal centrifugation¹³. The content of Na⁺/K⁺-ATPase was assayed⁵¹ and the activity in plasma membrane expressed as a percentage of the total in the various organelles.

The expression of H-2 histocompatibility antigens, generally accepted as plasma membrane components, has been measured by immune cytolysis and found to be at a minimum in S (ref. 15). To investigate the reason for this effect, we have titrated the number of antigenic sites

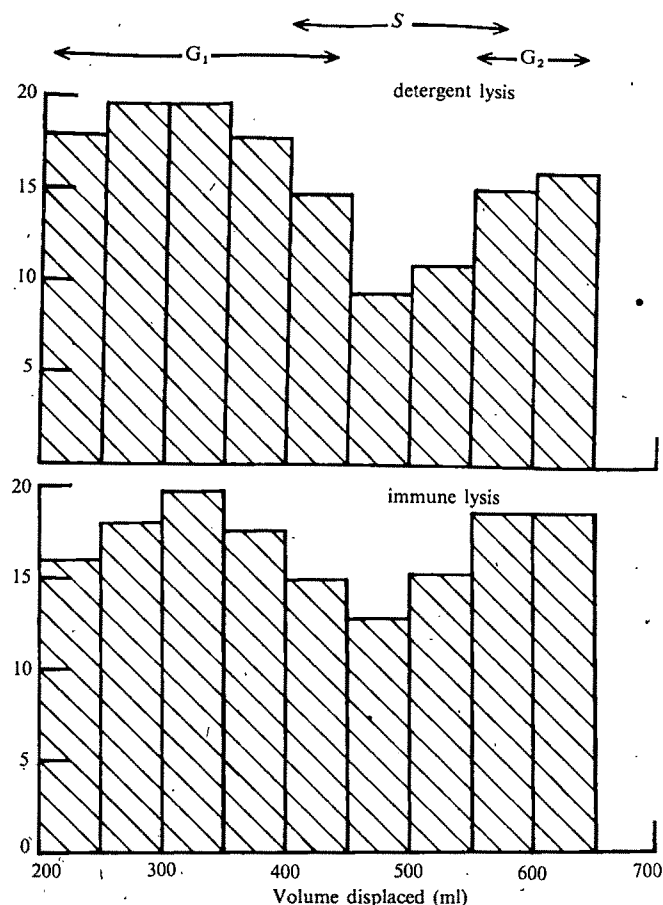


Fig. 5 Sensitivity to lysis during the cell cycle. P815Y cells (2×10^7 ml $^{-1}$) were incubated with $\text{Na}_2^{51}\text{CrO}_4$ (10 μCi ml $^{-1}$) for 40 min at 37° C, washed three times and separated by low-speed centrifugation. Pooled fractions were exposed to 0.004% Triton X-100 or 2% anti-H-2 serum plus complement¹⁵ in Tris-buffered (50 mM, pH 7.2) saline for 40 min at 37° C, spun, and radioactivity in supernatant and pellet was measured with a γ -scintillation counter. Sensitivity to lysis is expressed as the % of total ^{51}Cr in cells that is released. The periods of the cell cycle, based on Fig. 2, are indicated.

with ^{125}I -labelled antibody and have also assessed the number of sites by competition for antibody in the cytolytic assay⁴⁵. Both results show an increase in antigenic sites during early interphase. The decreased expression during S is therefore unlikely to be due to 'masking'⁴⁶ and must reflect some other cause.

One possibility is that interphase cells are less susceptible to immune cytotoxicity because of a non-specific decrease in fragility, and we accordingly measured the ease of lysis brought about by detergents, hypotonicity or freeze-thawing. In each case we observed (Fig. 5) a minimum of fragility during S, which matches the minimum of antigenic expression at this time¹⁵. It is also in keeping with the model proposed for plasma membrane assembly (Fig. 2c), in so far as mitotic and some G₁ cells are likely to be more fragile than other cells; this might explain the greater sensitivity of mitotic cells to virally-induced fusion⁴⁷. It is of course possible that there are additional reasons for the reduction in immune cytotoxicity during interphase; the decreased expression of H-2 antigens as measured by immunofluorescence⁴⁸, for example, cannot be attributed to this cause.

Conclusions

Our results are compatible with a model for plasma membrane assembly (Fig. 2c) in which the major components are synthesised and inserted throughout interphase. During this time the surface area increases up to a point in G₂ when the volume of the cell (assuming a sphere) has doubled;

the concentration of membrane components per unit of surface area is restored to the original G₁ value during cytokinesis. A 'thickening' or folding of the plasma membrane¹⁹ during interphase may account for the increased resistance towards immunological and other cytolytic agents; such changes are distinct from alterations in microvilli and other surface structures¹⁹ that may be involved in cell-cell or cell-substratum interactions in other cell types. Specific components like 5'-nucleotidase, Mg^{2+} -ATPase, H-2 histocompatibility antigens or amino acid transport proteins⁴⁹ are likewise synthesised and inserted during early interphase; whether this is true of enzymes such as Na^+/K^+ -ATPase or adenyl cyclase that show fluctuations in activity remains to be seen.

When cells in the G₀ or resting state are stimulated to re-enter the growth cycle, there is generally an alteration in surface architecture⁵⁰. The rapidity of onset (well before mitosis) may be related to the fact that early interphase is the time at which many surface components are synthesised and inserted.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Interpretation of the Hubble Diagram for Quasars

Setti and Woltjer^{1,2} have shown that the large scatter in the Hubble diagram for quasars (see Sandage³) may be greatly reduced if quasars with steep radio spectra and extended structures are considered alone. For this type of quasar there is a marked correlation between apparent optical magnitude and redshift, with a slope similar to that found for normal radio galaxies and the brightest galaxies in clusters.

The absence of such a correlation for quasars with flatter spectra may be attributed either to a broader dispersion in luminosity or to redshifts in these quasars, which are intrinsic to the source rather than a measure of cosmological distance. Although Setti and Woltjer prefer the explanation of luminosity dispersion, it is precisely this class of quasar for which Rowan-Robinson⁴ has presented independent arguments in favour of non-cosmological redshifts.

Here I extend the approach of Setti and Woltjer by considering in more detail the form of the radio spectra of a sample of the 166 quasars of known angular size and redshift (Miley⁵ and J. F. C. Wardle and G. K. Miley, to be published). Although the sample is slightly smaller than that used by Setti and Woltjer, the radio properties of the quasars included are considerably better determined.

For each source a radio spectrum has been compiled from measurements in the published literature, supplemented whenever possible by recent observations made at Jodrell Bank at 0.97 GHz (P. Haves, R. G. Conway and D. Stannard, to be published) and NRAO Greenbank at 2.7 and 8.1 GHz (J. F. C. Wardle and P. P. Kronberg, private communication). Each quasar has then been assigned a spectral classification according to the overall shape of its radio spectrum and the slope of the spectral curve evaluated at 3 GHz emitted frequency ($\alpha(3 \text{ GHz})$, defined in the sense that $S \propto f^\alpha$). Further details of this classification will be given as part of a comprehensive study of the radio polarisation properties of quasars which is being prepared by R. G. Conway, P. Haves, P. P. Kronberg, D. Stannard, J. Vallee and J. F. C. Wardle.

The three main categories considered here are: flat spectrum (thirty-two quasars), $\alpha(3 \text{ GHz}) \geq -0.3$; concave spectrum (twenty-six quasars), $\alpha(3 \text{ GHz}) < -0.3$, with a change of spectral index by $\Delta\alpha \geq +0.2$ in the range 0.5 to 5 GHz; steep spectrum (eighty-nine quasars), $\alpha(3 \text{ GHz}) \leq -0.7$ with a straight or convex spectrum.

This spectral subdivision has been chosen to reflect the degree of activity in quasars at radio wavelengths. The studies of Medd *et al.*⁶ suggest that the most violent radio variability is confined to the flat spectrum quasars, whilst the quasars with only a slight centimetre excess (concave spectrum) show only weak variability, and the steep spectrum quasars do not vary at all.

A formal classification has not been assigned to the 14 quasars in the sample with $-0.3 > \alpha(3 \text{ GHz}) > -0.7$ and a straight or convex spectrum. These sources are to be found among all three classes of activity, and presumably represent a borderline group which with more flexible splitting criteria could be redistributed amongst the major spectral categories. Five quasars with prominent maxima in the decimetre range also show no preferred degree of activity. As Medd *et al.* remark, this is rather surprising, as on the basis of many theories these sources might be expected to exhibit violent radio variability.

There is a striking correlation between spectral type and radio structure. 94% of the flat spectrum quasars have angular diameters of less than 3 arc s, whereas only 19% of the concave spectrum quasars and 20% of the steep spectrum quasars have such compact structures. Very long baseline interferometry⁷ suggests that many of the flat spectrum quasars remain unresolved on the scale of 10^{-2} arc s.

Table 1 Variation of Largest Angular Size with Redshift

Redshift range	Median LAS (arc s)	
	Concave spectrum	Steep spectrum
$z < 0.5$	40	55
$0.5 \leq z \leq 1.0$	15	20
$z > 1.0$	4	10

Both the concave and steep spectrum quasars show the decrease of largest angular size (LAS) with redshift which was first reported by Miley⁵. Although the data show considerable scatter (see ref. 5), there is a tendency for the median LAS of the concave spectrum quasars in each redshift range to be slightly smaller than that of the steep spectrum quasars (Table 1). In addition to this extended structure, the concave spectrum quasars frequently possess a compact radio component which is coincident with the optical nucleus and is responsible for most of the radiation at high frequencies. This component exhibits many of the properties commonly associated with the flat spectrum quasars.

Optical data for the quasars have been taken from the compilations of Setti and Woltjer² and De Veny *et al.*⁸. The Hubble diagram for the steep spectrum quasars in the present sample is similar to that presented by Setti and Woltjer^{1,2}, and shows a significant correlation between apparent V magnitude and redshift. As these authors suggest, the composite Hubble diagram for quasars of other spectral types does indeed show considerable scatter (Fig. 1), but if the quasars with flat spectra are considered on their own then there is again a marked correlation between apparent magnitude and redshift (Fig. 2).

The data for both the steep and flat spectrum quasars are consistent with a Hubble slope of 5 mag per decade of redshift. Although such a slope is not conclusive evidence for cosmological redshifts⁹, it is the value predicted on a Friedmann cosmology with $q_0 = +1$ and no luminosity evolution. Assuming this cosmology there is an important difference between the two types of quasar in that the mean absolute magnitude of the flat spectrum quasars is some 0.8 mag brighter than that of the steep spectrum quasars (with $H_0 = 50 \text{ km s}^{-1} \text{ Mpc}^{-1}$, the respective values are $-26.5 \pm 0.2 \text{ mag}$ and $-25.7 \pm 0.1 \text{ mag}$).

The Hubble diagram for quasars with concave spectra is shown in Fig. 3. It is not clear why this should be the only major class of radio quasar which fails to show a significant Hubble relationship. One possible explanation for the apparent steepness of the correlation between magnitude and redshift could be luminosity evolution in the sense that the high redshift quasars with concave spectra have systematically greater luminosities than those at low redshift.

The concave spectrum quasars possess a further optical peculiarity in that seven out of the twenty-six sources (27%) have prominent absorption features in their optical spectra, whereas the corresponding figures for the flat and steep spectrum quasars are four out of thirty-two (12%) and nine out of eighty-nine (10%), respectively. This presumably reflects the recent expulsion of material from the active nuclei of these quasars.

I thank Sir Bernard Lovell for comments and R. G. Conway,

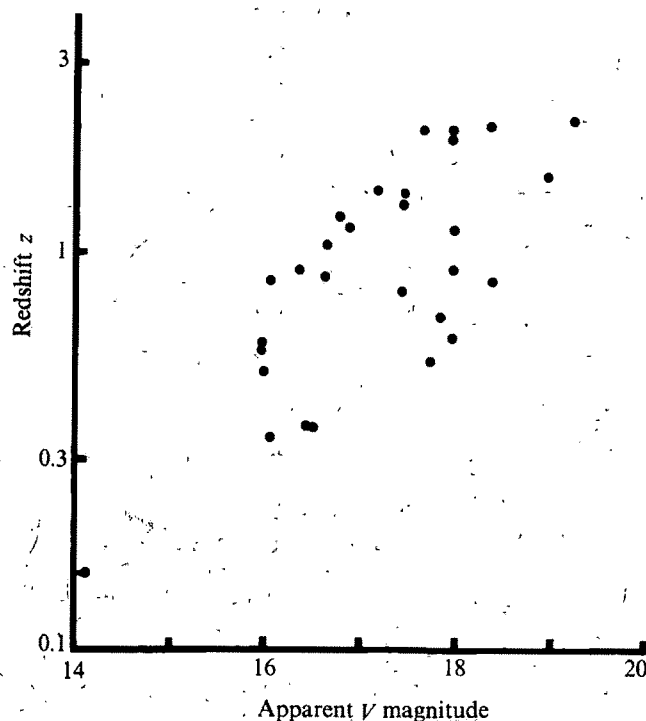


Fig. 2 Hubble diagram for quasars with flat radio spectra.

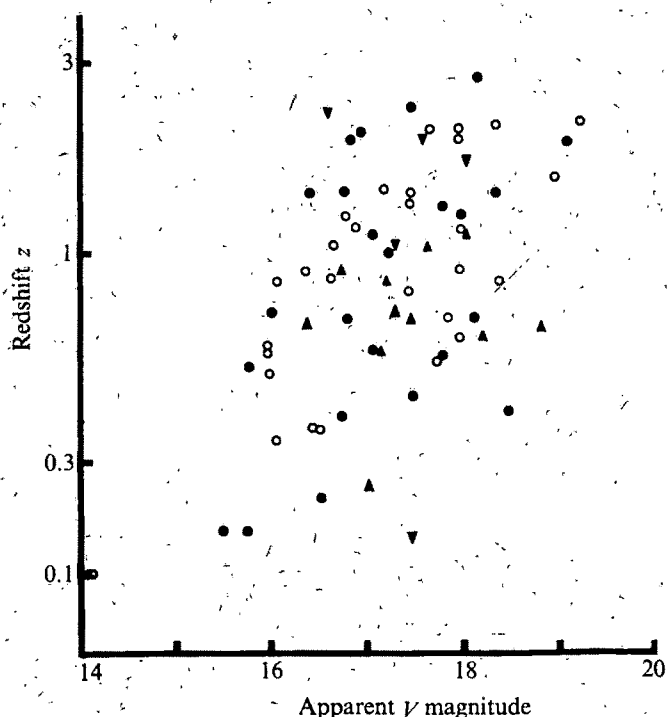


Fig. 1 Hubble diagram for quasars in the sample with measured V magnitudes and non-steep radio spectra. The flat spectrum quasars are represented by open circles, the concave spectrum quasars by filled circles, the straight spectrum quasars by triangles and the quasars with a single decimetric maximum by

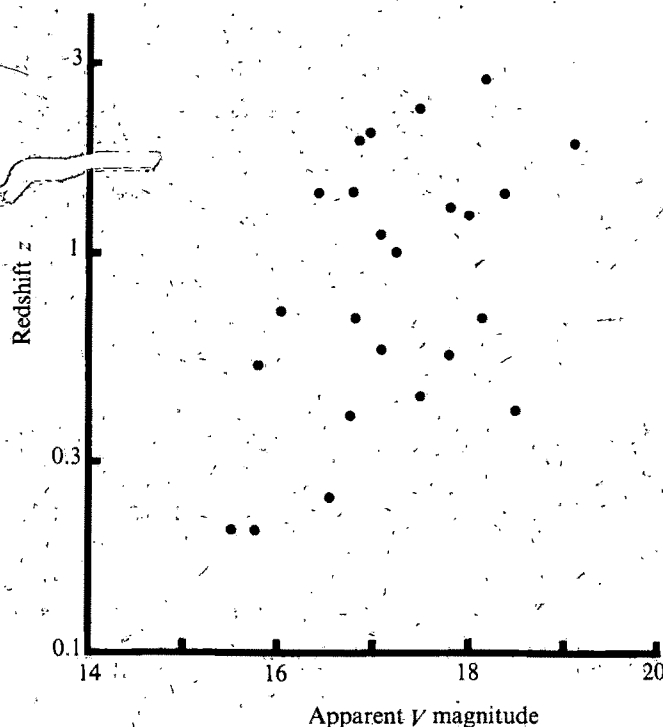


Fig. 3 Hubble diagram for quasars with concave radio spectra.

J. F. C. Wardle and P. Haves for discussions. J. F. C. Wardle and P. P. Kronberg communicated results in advance of publication and the Science Research Council provided a Research Fellowship.

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Median Valley Refraction Line, Mid-Atlantic Ridge at 37° N

THIS communication describes the results of a reversed seismic refraction line carried out with explosives and seabed receivers in the median valley of the Mid-Atlantic Ridge during July and August 1973. The work was part of a detailed investigation of a crestal area of the Mid-Atlantic Ridge south-west of the Azores by the Franco-American Mid-Ocean Undersea Study (FAMOUS) group.

There seem to be very few published results of seismic refraction lines shot in the median valley of the mid-ocean

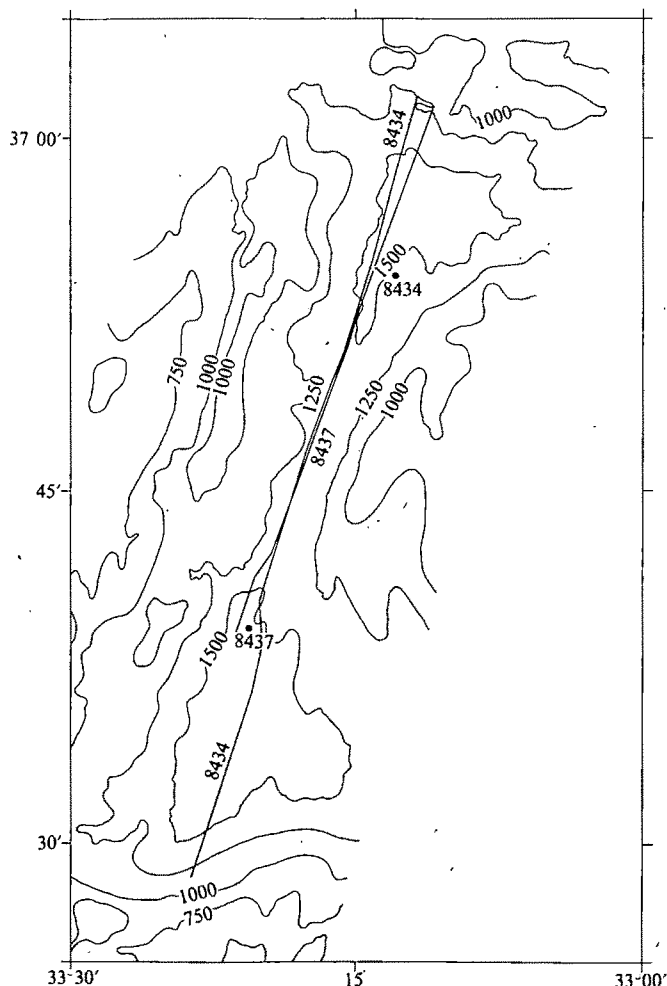


Fig. 1 Bathymetric chart of the median valley in part of the FAMOUS area showing the seismic refraction lines reported here; contours in uncorrected fathoms (from an unpublished chart produced by the Woods Hole Oceanographic Institution, courtesy of J. D. Phillips). The receiver position for each station is shown by a dot.

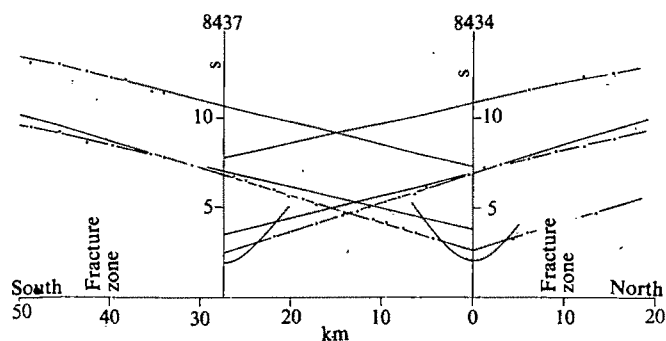


Fig. 2 Time-distance diagram of the two refraction lines. Points based on a multiple of the faster first arrivals are shown, but points from multiples of the slower first arrivals have been omitted. The curved lines were fitted to the direct water waves. See Table 1 for parameters of the straight lines.

ridge system¹⁻³. Such observations are necessary to provide constraints for models of ocean-crust genesis at mid-ocean ridges. The scarcity of seismic information about the near-surface structure beneath the axes of those mid-ocean ridges which have median valleys may be partly due to the remoteness of such regions but it is probably also a result of the difficulty of shooting conventional refraction lines there. The median valley in the FAMOUS area, for example, is less than 4 km wide except near the broad fracture zone valleys which offset it. It is difficult to prevent free-floating sonobuoys from drifting outside such a narrow target zone while a refraction line is being shot. The seabed recorders used in the present work, however, were free-fall pop-up devices⁴ which remained anchored to the seabed during the experiment so that the receiver positions remained fixed during each line.

Two refraction lines (Discovery stations 8434, 8437) were shot in opposite directions along the axis of the median valley in the FAMOUS area between two fracture zones (Fig. 1). Here the median valley is straight but rather short. Consequently some of the shots were fired over the wider parts of the median valley where it merges with the fracture zones or even over the fracture zone valleys themselves. Charge sizes were between 5 and 200 pounds for the first line and were fired at ranges up to 50 km from the receiver. Because of the strong arrivals thus obtained charges of only 5 or 25 pounds were used for the second line which was shot to a range of 43 km. The method of calculating horizontal range and travel time for the seabed receivers has been described elsewhere⁴. The range calculations made use of contemporary velocimeter information obtained nearby. Because of seafloor relief along the refraction lines the

Table 1 Lines Obtained by Least-squares Fitting

Station	Velocity (km s ⁻¹)	Intercept (s)	N
8434 (south)	6.47 ± 0.10	2.66 ± 0.04	15
	8.12 ± 0.40	3.59 ± 0.25	6
	(7.83 ± 0.53)	(7.20 ± 0.36)	7
8434 (north)	6.12 ± 0.36	2.69 ± 0.09	7
	6.29 ± 0.10	2.61 ± 0.05	13
	8.19 ± 0.38	3.72 ± 0.22	4
8437	(8.47 ± 0.81)	(7.70 ± 0.43)	4
	6.37 ± 0.07	2.71 ± 0.02	35
	8.16 ± 0.06	3.00 ± 0.08	10
All data	(8.02 ± 0.44)	(7.46 ± 0.27)	11

Errors are standard errors; N is the number of points on which each least-squares line is based. Results between parentheses are based on a multiple of the first arrival (see text).

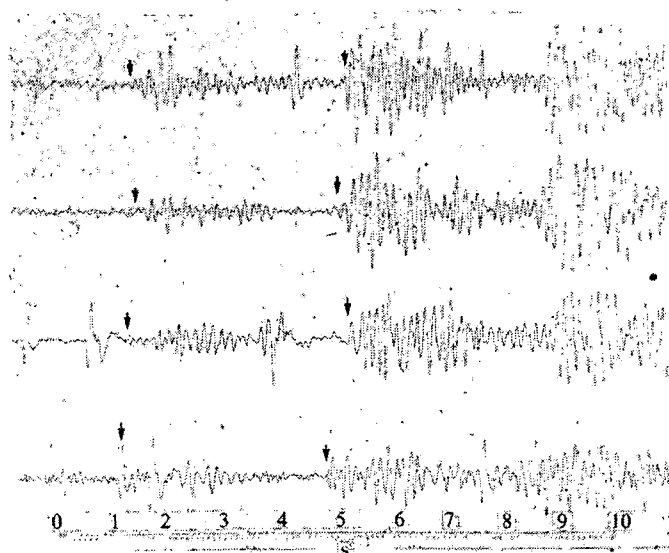


Fig. 3 Traces obtained from the seabed hydrophone for the four most distant shots of station 8437; shot-to-receiver range increases from top to bottom of the figure. The traces have been aligned so that a vertical line corresponds to a velocity of 8.0 km s^{-1} . ↓, Arrivals used to determine the velocity and intercepts of the second refractor. The occasional noise spikes are probably due to the acoustic transponder on the seabed equipment being triggered by local seismic noise. The records obtained at station 8434 were generally of better quality on account of the larger shot sizes.

travel times of ground waves were also corrected to the 1,700 fathom datum (3,193 corrected metres) assuming a basement velocity of 5.5 km s^{-1} . The resulting time-distance diagram is shown in Fig. 2 and the lines obtained by least squares fitting are shown in Table 1.

Table 1 and Fig. 2 show a well determined first refractor with a velocity between 6.12 and 6.47 km s^{-1} . The velocities and intercepts of the second refractor are less precisely determined essentially because they are based on fewer first arrivals than the first refractor. This is especially true of station 8437 where only four arrivals had the higher velocity and one of these had a poorly determined onset because of noise. It was possible to obtain independent confirmation of the existence of the second refractor, however, by considering multiples of the first arrivals due to a sea surface, or possibly a seabed, reflection. These arrivals, when observed at the seabed, are generally much greater in amplitude than their corresponding first arrival (Fig. 3). A similar procedure was carried out for station 8434.

It is particularly noticeable that the critical range beyond which first arrivals from the second refractor appear coincides at both stations with the deepest part of the cross-cutting fracture zone valley. It might therefore be argued that the arrivals with an apparent velocity of 8.2 km s^{-1} are actually due to a change in structure as the fracture zone is crossed, such as an upward dip of the first refractor. The northern half of station 8434, however, shows that this cannot be, since a normal first refractor velocity was observed there for arrivals passing across the fracture zone.

Statistically, since no measured velocity or intercept for stations 8434 and 8437 differs significantly from others in the same set all these values are assumed to be estimates of the same parameters. Thus best estimates of the velocity and intercept of each refractor were obtained using the reciprocal of the square of the standard error to weight each observation (Table 1). In practical terms this statistical argument is the same as making the assumption that both refractors are horizontal

It is readily apparent from a comparison of the observed and expected intercepts that the 6.37 km s^{-1} refractor does not outcrop at the seabed nor is it possible that a 4 or 5 km s^{-1} bed overlies it since then seabed arrivals should have been seen as first arrivals. If the ground wave arrival at shortest range is attributed to a seabed refractor then the calculated velocity of this refractor (3.26 km s^{-1}) represents a maximum for the seabed. Actually a 2.8 km s^{-1} seabed velocity was assumed, for the purpose of calculating a structure, since this velocity was observed about 30 km west of the median valley on another line shot with the seabed receivers.

Table 2 Mean Structure Beneath the Median Valley

Layer	Velocity (km s^{-1})	Thickness (km)	Depth of top (km)
1	1.50	3.19	0
2	2.80*	1.00	3.19
3	6.37	4.78	4.19
4	8.16	—	8.97

* Assumed velocity.

The calculated structure is presented in Table 2. This structure differs from that normally obtained in ocean basins only in the velocity of the seabed material, in the slightly lower velocity of the 6.37 km s^{-1} layer. There is no evidence of a velocity in the range normally attributable to Layer 2 but the topmost layer, which probably represents poorly consolidated or fractured volcanic material, may correspond to Layer 2A of Talwani *et al.*⁵. The velocity of the first refractor is remarkably close to that observed in the axial trough of the Red Sea³ out to a range of 45 km , but otherwise the observed velocities differ from earlier median valley lines^{1,2}.

I shall not discuss these results extensively here but broadly it can be said that a typical Layer 3 exists over a normal velocity upper mantle. The anomalous 7.4 km s^{-1} axial upper mantle of Le Pichon *et al.*³ and Ludwig *et al.*⁶ is not observed. It seems evident that mantle material, which in this case could conceivably represent the top of the asthenosphere, is no closer to the seabed beneath the FAMOUS area than it is elsewhere in the North Atlantic. The mantle velocity, although not precisely determined, appears to be higher than might be expected from a mixture of olivine *b* and *c* crystal axes, or even *c* axes alone, aligned along the median valley⁷, as required by the models of Francis⁸ and Whitmarsh⁹ for generating upper mantle anisotropy, taking into account the expected temperature and pressure (about $1,000^\circ \text{C}$, 2 kbar)¹⁰ at the base of the crust beneath the median valley. It is also noticeable that arrivals which have travelled across the fracture zones at the top of the 6.37 km s^{-1} layer do not exhibit any clear travel time anomalies.

This work forms part of a larger seismic study of the FAMOUS area which will be published in detail at a later date.

I thank those colleagues who assisted in the execution of the seismic lines at sea, especially J. Langford and A. S. Laughton.

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Attainment of Gigavolt Potentials by Magnetic Insulation

THE principle of my idea can be explained by Fig. 1, which shows a cross section through the proposed machine. The machine has two concentric conductors of toroidal symmetry which are placed within a toroidal magnetic field coil producing a magnetic field directed along the circular toroidal ring axis and varying in time. The space inside the inner conductor and in between the inner and outer conductor is a hard vacuum. The inner conductor is assumed to have a minor radius of r_i and the outer conductor a minor radius of r_a .

The inner conductor is not permitted to have any physical support in relation to the outside structure and thus has to be levitated. This can most easily be done by making the inner conductor or certain parts of it from a ferromagnetic substance. A properly applied auxiliary external feedback-controlled magnetic field coil, not shown in Fig. 1, can then keep the inner conductor stable in its position. The external conductor is surrounded by a toroidal magnetic field coil to be fed by a high current generator.

Both the inner and the outer conductor have a non-conducting gap. If the external coil is magnetised by the high current generator the magnetic field created can flow freely through these gaps first into the space between the outer and inner conductor and then into the space within the inner conductor. As a result the whole space inside the toroidal magnetic field coil will be filled with magnetic field.

If a cathode is placed within the gap of the outer conductor, emitting thermionic electrons, and if the externally applied magnetic field rises in time, then these electrons will be attached to and carried by the magnetic field lines moving towards the inner conductor. After reaching the inner conductor the electrons will detach themselves from the magnetic field lines and will form a surface charge on the inner conductor. The outer conductor, on the other hand, will be charged positively. The inner and outer conductors thus form a coaxial capacitor which is charged by the mechanism described up to some electrostatic potential.

There are, however, two important differences between the proposed machine and an ordinary capacitor.

(1) The charging up of an ordinary capacitor is usually carried out by some external voltage. Since the maximum attainable voltages are limited by dielectric breakdown in insulators, the maximum voltage available for charging a capacitor is limited regardless of the breakdown limitations within the capacitor itself. In contrast, charging up in the proposed machine is done entirely inductively and within a vacuum, thus eliminating the need for a high voltage source.

(2) The maximum voltage attainable in an ordinary capacitor, again, is dictated by dielectric breakdown. But for the proposed machine the situation is governed by a different principle. The externally applied axial magnetic field rises in proportion to the radial electric field resulting from the charging of the inner conductor and is thereby directed perpendicular to the radial electric field and parallel to both conducting surfaces. In this case, as long as the axial magnetic field

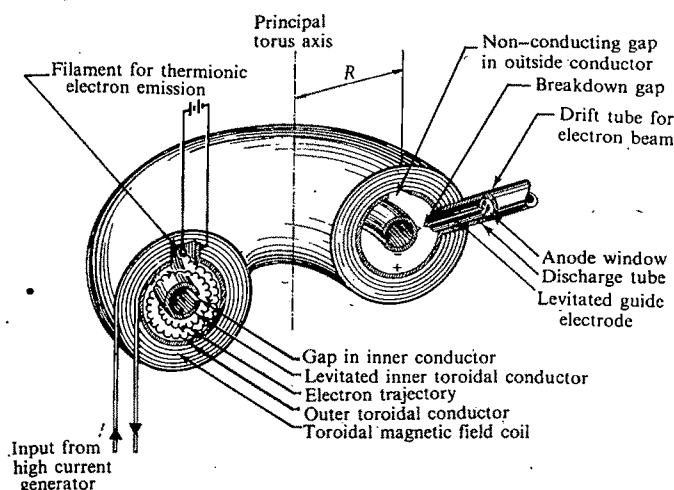


Fig. 1 Cross section through the toroidal machine described in the text.

strength $H >$ the radial electric field strength E (both measured in c.g.s. units) the magnetic field acts as an insulator with no dielectric breakdown limitations¹⁻⁴.

Because of the large magnetic fields attainable it is to be expected that the type of magnetically insulated capacitor described can be charged up to very high potentials. I assume, for example, that the magnetic field reaches a value of $H = 10^5$ gauss. The condition $E < H$ then means that $E < 3 \times 10^7$ V cm⁻¹. Therefore, for a gap between the inner and outer conductor which is assumed to be $r_a \approx r_i \sim 30$ cm the voltage of the capacitor would be $V \lesssim 10^9$ V. Furthermore, the energy stored in such a device would be considerable. If, for example, the volume occupied by the electric field is 1 m³ (10⁶ cm³), which is a rather modest volume if compared with conventional capacitors, then an energy $\epsilon \lesssim 40$ MJ could be stored. The discharge time τ of such a capacitor is of the order (volume)^{1/3}/velocity of light $\sim 3 \times 10^{-9}$ s. The discharge current is given by $I \sim \epsilon/V\tau \sim 10^7$ A. These values are far beyond the capability of any conventional machine operating with ordinary capacitors. Moreover such a machine can quite conceivably be built substantially larger, for example, by a factor of 100 in volume. This would lead to a stored electrostatic energy of several GJ. But even in this case the magnetisation of the field coil, and thus inductive charging, could still be carried out with a unipolar d.c. machine.

After the voltage has reached its peak value, whereupon E begins to exceed H , controlled breakdown will occur at a properly placed gap between a protrusion of the inner conductor and an auxiliary guide electrode in the form of a rod. As shown in Fig. 1 this guide electrode is placed in the centre of a coaxial conducting discharge tube. For this configuration the guide electrode has to be levitated, which again can be most easily achieved by making the guide electrode of some ferromagnetic material to be suspended by feedback-controlled external magnetic field coils. The coaxial conducting discharge tube is connected to, and at the same potential as, the outside toroidal conductor. During the charging up of the inner toroidal conductor, the guide electrode must be kept at the same potential as the outer conductor and the discharge tube. This will most probably happen automatically because of a small field emission current from the guide electrode onto the conducting discharge tube.

After breakdown has occurred in the breakdown gap, an intense beam of electrons will propagate along the surface of the guide electrode in a way similar to that observed by Bennett *et al.* for a dielectric rod⁵. What probably happens is that by action of the beam, some plasma will be formed on the surface of the guide electrode, cancelling the space charge of the electron beam emitted from the inner conductor. In propagat-

ing along the surface of the guide electrode the electron beam will then magnetically insulate itself against radial breakdown towards the coaxial tube. If, for example, the guide electrode has a diameter of $R=1$ cm and the electron current is 10^7 A, a self-magnetic field of $H \sim 2 \times 10^6$ gauss will be established by the beam, which is more than sufficient to ensure complete magnetic insulation of the beam against radial breakdown. If, for example, the voltage is $V \sim 10^8$ V an electric field of $E \sim V/r \sim 10^8$ V cm $^{-1} \approx 3 \times 10^5$ e.s.u. is set up, so that clearly $E < H$.

After it reaches the end of the guide electrode the front of the electron beam faces the anode window. At the high energies contemplated the electron beam will pass through the anode window into the drift tube without any appreciable energy loss.

The power of the electron beam is $\sim IV = 10^{16}$ W. Furthermore, since the inductive charging can be done in a fraction of a second, the machine can work in a rapid sequence at very high average power levels that are unattainable in conventional particle accelerators.

The charging current I_c can be computed from the condition $I_c \tau_c = I \tau$ where τ_c is the charging time. If, for example, $\tau_c = 10^{-2}$ s it follows for the above values of I and τ that $I_c = 3$ A, which can easily be generated by thermionic emission. The power for the charging process is of the order $\sim I_c V = 3 \times 10^9$ W and could be drawn from a conventional a.c. power source. For large power levels a unipolar generator could be used.

The two most important applications of the machine described are for controlled thermonuclear fusion and for the collective acceleration of ions to ultrahigh energies.

(1) It is known that thermonuclear fusion can be achieved by utilising the concept of thermonuclear micro-explosions if the following conditions can be met: (a) an energy source must be available to deliver an energy of $\sim$ several MJ within 10^{-8} s; (b) the energy source must be capable of concentrating the energy into a volume which is a small fraction of 1 cm ^{3} ; (c) after concentration into such a small volume the energy has to be dissipated in heating up the thermonuclear material to be placed within the small volume.

A machine of modest dimension can easily meet the first condition. Since the energy is delivered in the form of an intense relativistic electron beam it can be concentrated into a very small volume if the strong self-magnetic forces acting on the beam are utilised. In this way the second condition can be met. The third condition can be very probably fulfilled by the collective beam-plasma two-stream instability¹. The energy and power which can be delivered by such a machine may even make possible the release of thermonuclear energy from the D-D reaction.

(2) The prospect of collective ion acceleration⁶ becomes especially interesting at the contemplated electron beam energies and intensities. The effect of collective ion acceleration can be most easily visualised in the following way. If an ion is placed in an intense stream of electrons, then by interaction with the beam it will eventually acquire the same γ value. But because, for example, a hydrogen ion has a mass $\approx 1,800$ times larger than the electron, energies for the same γ values are larger by the same amount. Since the electron energies range up to 10^9 eV it follows that hydrogen ions could be accelerated up to $\sim 10^{12}$ eV = 1,000 GeV.

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Acceleration and Injection of Highly Relativistic Electrons during the August 7, 1972, Solar Flare

THE 3B flare of August 7, 1972, has been one of the largest of the present solar cycle and, thanks to the favourable conditions for particle propagation (the position of the flare on the Sun was 14° N, 37° W) and to the time of the day it occurred, one for which a large quantity of data is or will be available.

Mathews and Lanzerotti¹ have reported an observation of relativistic protons at Earth. Their results show that relativistic particles are accelerated and ejected into interplanetary space before the H α maximum phase is reached and in near coincidence with the white light phase.

Highly relativistic electrons from that flare have been observed in outer space (~ 33 Earth radii) by spacecraft. The characteristics of a former version of the detector have been described by Dilworth *et al.*². The present one has an energy threshold for electrons of about 20 MeV, taking into account the total efficiency of the instrument in the configuration it was on August 7, 1972. Figure 1 shows the time profile of the onset of the flare electrons. The integrated counting rate is transmitted every 32 s, but a statistically significant profile can be obtained only integrating over 128 s, which correspond to four telemetry frames. The first flare electrons are observed only between 1535 and 1537 UT, that is at least 5 to 10 min after the Calgary and Sulphur Mountain protons.

There are at least two instances in which MeV electrons and GV protons have been observed almost contemporaneously at Earth, in the well studied flare of July 7, 1966 (ref. 3) and on February 25, 1969 (ref. 4). The solar longitude of this latter event was also 37° W and the high energy electrons were observed by means of the same experimental technique². A time lag in the arrival time of flare-produced relativistic electrons and protons is not therefore a common feature of solar events.

Figure 2 shows schematically the time history of the relevant phenomena which occurred on August 7, 1972. The time scale is the time at the Sun (SUT) and particles are supposed to have travelled along the computed Archimedes spiral line¹. The GHz radio bursts⁵ and the hard X-ray emission⁶ are sure signs of relativistic electrons moving in the solar magnetic fields. Depending on the frequency, the radio burst rise times are of 11 to 15 min and the maximum intensity is reached at 1514 SUT. Hard X rays have rise times of about 8 min and a maximum at 1513 SUT. The time of maximum of the GHz radio bursts, of the hard X rays and of the white light flare¹ (this latter phenomenon indicating precipitation of accelerated protons and electrons and heating of the photosphere) all coincide within 2 min. The chromospheric H α flare, on the contrary, has a maximum at 1526 SUT (ref. 7), but this does not seem to be strictly connected with particle acceleration. The 4 GV protons leave the Sun at 1515 SUT. Acceleration of relativistic particles has therefore taken place before this time and from the radio and X-ray rise times we can conclude that it has lasted about 8 to 10 min. Unless unorthodox mechanisms are considered, this duration of

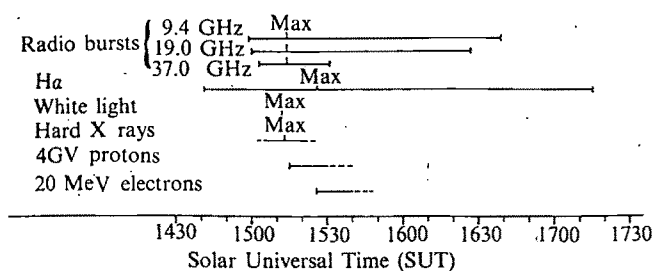


Fig. 1 Time profile of the onset of the >20 MeV electrons

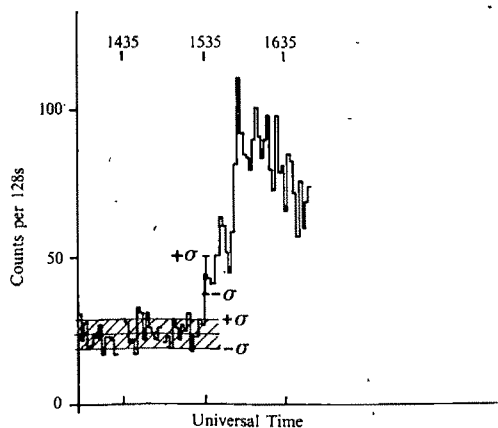


Fig. 2 Schematic time history of the main events of the August 7, 1972, solar flare.

acceleration is too long to produce the electrons observed at the Earth. Fürst *et al.*⁸ have analysed the 17 and 35 GHz bursts and find that the magnetic field in which the electrons radiate must be of the order of 1,000 gauss. Svestska⁹ has shown that there is a strict relation between the magnetic field, the duration of acceleration and the electrons high-energy cutoff. For a 1,000 gauss field, he computed a cutoff of 18 MeV for a duration of 1 min. This difficulty can be overcome by supposing that several accelerations (at least four) have taken place during the ~10 min rise time of the radio and X-ray bursts, each acceleration lasting less than 1 min. Evidence for this is supplied by the time profiles in the radio and X-ray frequency bands, since the rise to maximum intensity is not monotonous, but at least four peaks are identifiable, each with rise times of less than 1 min.

This multiple acceleration cannot, however, explain the time lag at the Earth between protons and electrons. If a very fine structure of the interplanetary magnetic field is not responsible for the delay in the arrival time of the first electrons, these must spend 5 to 10 min after acceleration in the solar corona, in a region where radiation energy losses are not large. The implication is that, since the times of acceleration and of injection into interplanetary space may not always coincide, care must be taken in applying the propagation theories to solar particle events. Furthermore, if the time delay in the onset of the relativistic electrons means that they spend this time in the solar corona, not only their injection time but also the longitude of injection can be different from that of the protons.

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Monocarboxylic Acids in Murray and Murchison Carbonaceous Meteorites

THAT carbonaceous meteorites contain organic substances has been known for more than a century, and during this time controversies developed concerning whether or not this organic material was a product of extraterrestrial life. Within the past few years studies of carbonaceous meteorites have provided solid evidence that certain organic compounds are indigenous and were most likely produced by non-biological, chemical syntheses¹⁻⁷. These studies have emphasised the occurrences of amino acids and hydrocarbons in two C2 carbonaceous chondrites, the Murray and the Murchison. We have now found in specimens of both of these meteorites straight and branched-chain monocarboxylic acids having two to eight carbon atoms. Although many of these acids are of biological significance, the distribution of compounds in these meteorites supports the proposition that they, like the amino acids and hydrocarbons, result from non-biological, chemical syntheses.

The outside fusion crusts of both meteorites were carefully removed. Interior pieces were finely ground in a mullite mortar with a pestle. A 6.1 g sample of Murray and a 5.3 g sample of Murchison were each processed separately using the following procedure. The pulverised sample was refluxed with 30 ml of methanolic potassium hydroxide (10:1 v/w) for 3 h, with stirring, in a 100 ml round-bottom flask. A reflux condenser with a drying tube containing potassium hydroxide pellets and Drierite was attached to the flask. After cooling to room temperature, the contents of the reaction flask were transferred and centrifuged in two 50 ml Teflon test tubes. The supernatant was decanted into a separatory funnel containing 30 ml of distilled water. The resultant alkaline solution, after three extractions with 15 ml portions of dichloromethane, was collected in a 100 ml round-bottom flask and evaporated to dryness under reduced pressure. Cold, concentrated hydrochloric acid was added to the solid residue until the resulting solution reached pH 1, while the flask and its contents were cooled in an ice-water bath. The acidified solution was extracted five times with 1 ml portions of dichloromethane. The combined extracts were dried over 0.5 g anhydrous sodium sulphate. The carboxylic acid content of this solution was determined by gas chromatography and by combined gas chromatography-mass spectrometry.

Identification of monocarboxylic acids in both the Murray and Murchison meteorites is based on (1) coincidence of gas chromatographic retention times between sample monocarboxylic acids and authentic standards, and (2) equivalence of mass spectra of the sample compounds with the mass spectra of standards obtained in this laboratory and from the literature^{8,9}. Interpretation of mass spectra of these monocarboxylic acids is relatively straightforward¹⁰. The following ten monocarboxylic acids are securely identified based on the criteria given above: acetic acid; propanoic acid; 2-methylpropanoic acid; butanoic acid; 3-methylbutanoic acid; pentanoic acid; 4-methylpentanoic acid; hexanoic acid; heptanoic acid; octanoic acid.

In addition five monocarboxylic acids are only tentatively identified because of the lack at this time of authentic standards with which to obtain gas chromatographic retention times. These compounds, however, have mass spectra which resemble published mass spectra⁸: 2,2-dimethylpropanoic acid; 2-methylbutanoic acid; 2-methylpentanoic acid; 3-methylpentanoic acid; 4-methylhexanoic acid.

Two of these compounds (2-methylbutanoic acid and 3-methylpentanoic acid) seem to be present in the standard as impurities (Fig. 1). The presence of two or three addi-

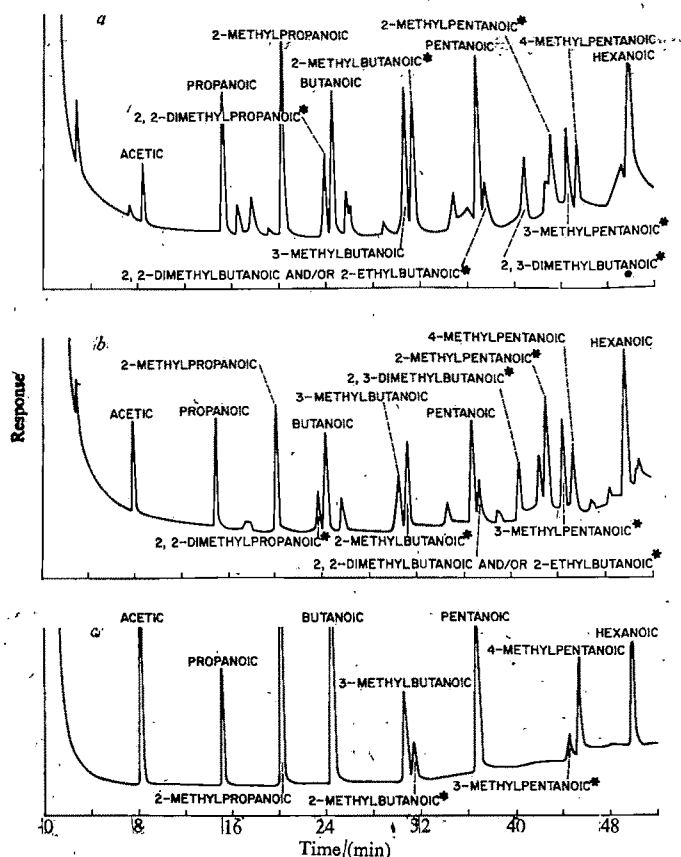


Fig. 1 Gas chromatograms of monocarboxylic acids in Murray (a) and Murchison (b) meteorites compared with a mixture of standard acids (c). *, Tentative identification. 2-Methylbutanoic acid and 3-methylpentanoic acid seem to be impurities in the standard. Chromatographic conditions: Perkin-Elmer 900 (flame ionisation) with stainless steel capillary column (46 m $\times$ 0.05 cm internal diameter) coated with UCON L8-550 x-H, PO₄ (ref. 11). Temperature programmed at 1° min⁻¹ from 70° to 120° C.

butanoic acid and/or 2-ethylbutanoic acid) is indicated based on rationalisations of their mass spectra. Figure 1 compares the gas chromatograms of the monocarboxylic acids recovered from both the Murray and Murchison meteorites with a standard. The chromatograms show compounds only to hexanoic acid. With the chromatographic conditions used, 4-methylhexanoic acid, heptanoic acid and octanoic acid had long retention times and showed peak broadening. The possible presence of monocarboxylic acids with more than eight carbon atoms is a subject of our continuing research.

The occurrence of short-chain monocarboxylic acids in carbonaceous meteorites has not been reported previously. But long-chain fatty acids, higher than about C₁₄, were reported to be present in the Orgueil meteorite by both Meinschein¹² and Nagy and Bittz¹³. In this earlier work even-carbon-numbered fatty acids dominated the mixtures and there was no mention of the occurrence of branched-chain fatty acids. Hayes¹⁴ suggests that the results may, in part, be accounted for by terrestrial, biological contamination. In our work we also looked for the long-chain fatty acids. Gas chromatographic evidence suggested the presence of tetradecanoic acid, hexadecanoic acid and octadecanoic acid (as methyl esters resulting from the esterification procedures used) in surface samples of Murchison meteorite. But no evidence could be found for these compounds when interior portions of the meteorite were studied.

The concentration of short-chain monocarboxylic acids recovered from the Murray and Murchison meteorites ranges from about 10 to 60 μ g g⁻¹ for

This concentration is about an order of magnitude larger than the concentration of amino acids recovered from the same meteorites (but different specimens)^{1,3}. The state of the monocarboxylic acids within the meteorite samples is not known at present; they may occur as free acids or esters or possibly as salts.

In the Murray and Murchison meteorites the distribution of monocarboxylic acids is remarkably similar. Both straight and branched-chain monocarboxylic acids are present. In fact, all the possible monocarboxylic acid isomers containing two, three, four, and five carbon atoms are accounted for. Of the eight possible monocarboxylic acids containing six carbon atoms, at least five are present and perhaps seven can be accounted for. The presence of so many isomers of these low molecular weight, monocarboxylic acids is comparable to the similar isomeric distribution of amino acids having four and less carbon atoms². It seems evident that a random chemical synthesis must have been responsible for generating both populations of molecules. Whether a relationship exists between the two populations is not known at present.

The characteristic even-carbon-numbered predominance of natural, biological populations of monocarboxylic acids¹⁵ contrasts with the distribution of acids found in the meteorites (Fig. 1) wherein both even and odd-carbon-numbered molecules are about equally abundant, and branched-chain acids are as common as straight-chain acids. Clearly, the difference in distributional patterns between the acids in the meteorites and acids in biological materials rules out the remote possibility that the acids in the meteorite resulted from terrestrial, biological contamination.

The finding of these monocarboxylic acids in meteorites has important implications for chemical evolution. In synthesis experiments Miller¹⁶ formed formic, acetic and propanoic acids when a primitive-type Earth atmosphere was exposed to a dark discharge. Eck *et al.*¹⁷ predicted on theoretical grounds that monocarboxylic acids in the range considered in this paper (C₂ to C₆) could be formed inorganically under equilibrium conditions, and that there would be little difference in concentration between straight and branched-chain isomers. Our meteorite results support this prediction with regard to isomer distribution. Allen and Ponnamperuma¹⁸ reported the production of C₂ to C₁₂ monocarboxylic acids in a methane-water mixture which was exposed to a semicorona discharge. The following acids were identified: acetic; propanoic; butanoic; 3-methylbutanoic; pentanoic; and 4-methylpentanoic. At carbon numbers greater than six, only branched-chain carboxylic acids were detected. Our meteorite studies suggest that the monocarboxylic acids found may have been generated by a naturally occurring, chemical synthesis; indeed, the results provide strong support for the chemical evolution theory.

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Pleistocene Human Occupation and Extinct Fauna in Cloggs Cave, Buchan, South-east Australia

A STRATIFIED and undisturbed occupation deposit containing stone and bone tools and a rich faunal assemblage has been discovered in a limestone cave at Buchan, in eastern Victoria (latitude 37° 31' S, longitude 148° 10' E). This is the first Pleistocene occupation site in which bone is preserved, yet found in eastern Australia.

Part of the deposit has been excavated, to a depth of 2 m, where massive slabs of rock fall were encountered. The lowest level excavated yielded extinct fauna, including a mandible *in situ* of the extinct giant kangaroo, *Sthenurus orientalis*. Immediately above the horizon containing extinct fauna were traces of human occupation, in the form of stone tools. Charcoal associated with the lowest tools was dated to 17,720 ± 840 BP (ANU-1044).

The tool assemblage compares very closely with that of the 8,000 yr-old levels of the Rocky Cape cave in northern Tasmania, excavated by Jones¹. Both assemblages comprise pebble tools, steep-edged scrapers and bone awls, all of which reflect the manufacture of skin rugs and of wooden implements such as spears.

The Buchan cave was apparently vacated about 8,000 yr ago, a date of 8,720 ± 230 BP (ANU-1001) having been obtained on charcoal from a hearth level only 15 cm below the present floor of the cave. The rock shelter outside the cave was utilised, however, in more recent times.

The vacation of the dark, but warm and dry, inner cave may have occurred in response to the climatic amelioration at the end of the Glacial Period, but the faunal evidence shows that there was a basic climatic and vegetational stability over the period represented by the cave deposit, that is, from before 18,000 BP to 8,000 BP. The species represented inhabit grassland, open woodland and dry sclerophyll forest habitats, together with wet grassy hollows and swampy alluvial flats such as are found along the Buchan River today.

Flotation techniques were used in processing the cave

deposit, and by this means some vegetable material such as leaves and wood was recovered. Coprolites were also found, and it has been possible to identify the species of grass eaten by the herbivores found at the site.

Work on Cloggs Cave thus has important implications for the study of the palaeoenvironment as well as for the pre-history of Australia, and is continuing under the aegis of the Australian Institute of Aboriginal Studies.

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BIOLOGICAL SCIENCES

Translation of Collagen mRNA from Chick Embryo Calvaria in a Cell-free System derived from Krebs II Ascites Cells

COLLAGEN is a helical molecule composed of three polypeptide chains (α chains) each with a molecular weight of approximately 95,000. The polypeptides are synthesised separately as precursor chains containing additional amino acids at the NH₂ terminal end¹⁻³. These pro α chains aggregate to form procollagen which is then secreted from the cell^{3,10}. Procollagen peptidase removes the NH₂ terminal segment from the soluble procollagen and the collagen is then deposited in extracellular fibres¹¹.

Although there have been several recent reports of cell-free synthesis of collagen, these describe the continuation of collagen synthesis on pre-existing polysomes using disrupted cells from embryonic chick wings and legs^{6,7} and from L-929 fibroblasts¹². We describe here the preparation of mRNA from 15-d chick embryo calvaria, and its translation in a true heterologous system derived from pre-incubated Krebs II ascites cells. Unlike previous reports, our system depends on the addition of exogenous RNA for protein synthesis.

The level of functional mRNA in the total RNA extracted from the calvaria was determined by its ability to direct the incorporation of radioactive proline into trichloroacetic acid (TCA)-tannic acid-precipitable material in a cell-free system derived from preincubated Krebs II ascites cell extracts. Components of the cell-free system are listed in Table 1. Proline incorporation had a magnesium optimum of 3 mM and a broad potassium optimum with a peak at 55 mM. As has been previously noted¹³, low concentrations of EDTA stimulated incorporation. Ascorbic acid increased incorporation by 10% and was included routinely in the reaction mixture.

In a standard reaction, proline incorporation was linear for 30 to 40 min and gradually reached a plateau so that at 60 min the incorporation was 50–100 times greater than background (without added mRNA). The extent of incorporation was directly proportional to the amount of calvaria RNA added to the reaction mixture. We were unable to saturate the system with the calvaria RNA under the assay conditions used.

The Krebs II ascites system was developed by Kerr *et al.*^{14,15} and Mathews and Korner¹⁶. While they found that protein synthesis in the ascites system was independent

of exogenous tRNA, Aviv *et al.*¹⁷ observed dependence when exogenous tRNA was added.

After initial experiments in which we observed that exogenous tRNA had a slight inhibitory effect on the Krebs II system we increased the preincubation period of the ascites S30 extract. This increase lowered the background incorporation five-fold to 300 c.p.m. and made the extent of incorporation sensitive to the addition of tRNA (Table 1). Optimal tRNA stimulation was observed after 100 min of preincubation. The cause of ascites tRNA inactivation during the extended preincubation is unknown. Our findings indicated that differences in the preincubation procedure can account for the discrepancy in previous reports concerning the tRNA dependency of the Krebs II ascites system.

The protein synthesised was identified by subjecting the product to digestion by bacterial collagenase. The specificity of the enzyme was determined by its failure to digest a whole chick embryo extract labelled with ³H-tryptophan, an amino acid absent from collagen. By susceptibility to

Table 1 Effect of Increasing the S30 Extract Preincubation Time on tRNA Dependency

Pre-incubation time (min)	μg tRNA* added	TCA-tannic acid precipitated ³ H-proline (c.p.m.)	% of control
45	—	8,156	100
	7.5	6,678	82
	15.0	7,160	88
100	—	4,550	100
	7.5	8,390	184
	15.0	13,550	305
120	—	4,100	100
	7.5	7,700	188
	15.0	9,700	237

An S30 extract was prepared from Krebs II ascites cells as described¹⁶ except that the preparation was dialysed against buffer. The S30 extracts were prepared identically with the exception of the length of the preincubation period. RNA was prepared from the calvaria of 15-d embryonic chicks (Truslow Farms). The tissue was removed, placed in liquid nitrogen and ground to a fine powder in a mortar and pestle. The powder was suspended in 10 volumes of buffer containing 50 mM Na acetate, pH 5.0, 1 mM EDTA, 1% bentonite and 0.5% Sarkosyl and extracted at 50° C for 2 min with an equal volume of phenol:chloroform:isoamyl alcohol (50:50:1). The aqueous phase was re-extracted twice more. RNA was precipitated with two volumes of ethanol and 0.03 volumes of 4 M NaCl. The RNA was collected by centrifugation and dissolved in water at a concentration of 60 A₂₆₀ ml⁻¹ and stored in liquid nitrogen. The tRNA was extracted from 12-d embryonic chick wings and legs by the same method. The aqueous phase was precipitated with 2 volumes of ethanol and 0.1 volume of 20% K acetate. The RNA was collected by centrifugation, washed three times with 70% ethanol, and dissolved in 10 mM Na acetate buffer, pH 4.5, containing 1 M NaCl. The supernatant was chromatographed on DEAE by the method described³⁰. The tRNA was collected by ethanol precipitation, dissolved in 10 mM Na acetate buffer, pH 4.5, containing 10 mM MgCl and 0.2 M NaCl at a concentration of 30–60 A₂₆₀ ml⁻¹ and stored at –20° C. Concentration of RNA was estimated by A₂₆₀; 25 A₂₆₀ 1 mg ml⁻¹. A standard 50 μl reaction mixture contained 0.50 A₂₈₀ units S30 extract, 0.09 A₂₆₀ units tRNA, 0.08 A₂₆₀ units calvaria RNA, 16 μg denatured lathyritic chick collagen²⁸, 160 μg creatine phosphate, 8 μg creatine phosphokinase, 3.2 μg ascorbic acid and 3.2 mM Mg acetate, 85 mM KCl, 44 mM Tris-HCl, pH 7.5, 1 mM ATP, 0.16 mM GTP, 0.8 mM CTP, 0.13 mM EDTA, 4.6 mM 2-mercaptoethanol, 40 μM nineteen cold amino acids and 2 μM 3,4-³H-proline, neutralised (1.37 × 10⁴ c.p.m. pmol⁻¹). The reactions were incubated at 37° C for 60 min. A 200-fold excess of cold proline was added to the reaction mixture and incubation was continued for an additional 20 min to chase ³H-proline from prolyl-tRNA. A 1 ml sample of cold 10% TCA containing 0.5% tannic acid was added and the reaction mixture chilled. The samples were filtered on Millipore filters which had been soaked for 30 min in 5% TCA containing 4 mM proline. The filters were washed with cold 5% TCA containing 0.25% tannic acid, dried at 80° C for 30 min and counted in a toluene-Liquifluor cocktail in a Beckman scintillation counter.

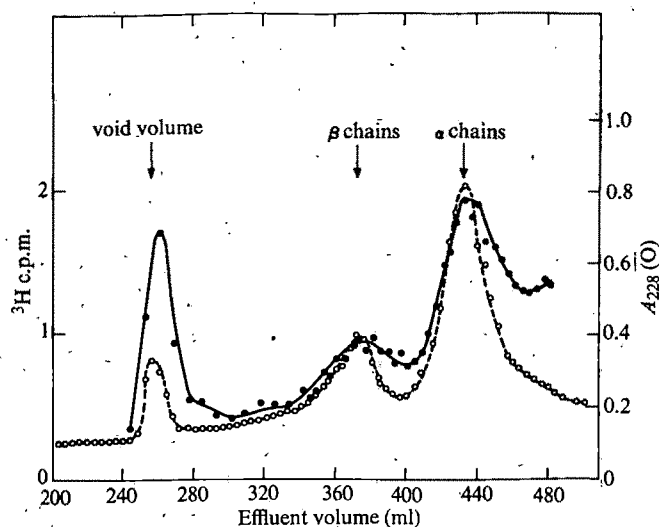


Fig. 1 Molecular sieve chromatography of the *in vitro* synthesised protein. A reaction mixture, thirty-fold the standard reaction (Table 1), was incubated for 60 min at 37° C. The precipitate formed during the incubation was collected by centrifugation (10,000g for 10 min) and dissolved in buffer (50 mM Tris-HCl, pH 7.5) containing 8 M urea and 10 mM mercaptoethanol. 5 mg of purified lathyritic chick skin collagen^{28,29} was added and the solution was heated for 30 min at 40° C. CaCl₂ was added to a final concentration of 1 M. The sample was applied to a 6% agarose column (1.5 × 200 cm) equilibrated with 50 mM Tris-HCl, pH 7.5, buffer containing 1 M CaCl₂. A Buchler peristaltic pump reduced the flow rate to 20 ml h⁻¹. Fractions (4 ml) were collected and the A₂₂₈ of each fraction was measured. Aliquots (1 ml) were counted in Aquasol (New England Nuclear) in a Beckman scintillation counter: (●) radioactivity; (○) A₂₂₈. The collagen molecule contains three polypeptide chains. Collagen of skin, bone and tendon contains two identical chains termed α1, and a third chain which is a different gene product, α2. The formula for the complete molecule is (α1)₂α2. The collagen of cartilage is composed of three identical chains, termed (α1)₃. α chain dimers can be observed, and these are termed β chains. A β component may be composed of two α1 chains (β₁₁), or of one α1 and one α2 chain (β₁₂).

collagenase digestion, it was estimated that 55% of the products synthesised in the *in vitro* system was collagen (Table 2).

A more rigorous identification of the protein product was effected by isolating the radioactive protein from a large scale reaction mixture. The reaction was terminated by the addition of EDTA to 50 mM, and immediately chilled. The precipitate which formed during incubation was collected by centrifugation and solubilised by heating to 40° C in buffer (50 mM Tris-HCl, pH 7.5) containing 8 M urea and 10 mM 2-mercaptoethanol. Samples of the supernatant and the solubilised precipitate were chromatographed separately on molecular sieve columns of 6% agarose. While no proteins with a molecular weight greater than 20,000 were present in the reaction supernatant, the solubilised precipitate contained three high molecular weight proteins (Fig. 1). Two of these radioactive proteins co-chromatographed with the α and β chain components of the chick carrier collagen used as markers.

CM-cellulose chromatography identified two proteins as α1 and α2 respectively, on the basis of their co-elution with chick carrier collagen (Fig. 2). Therefore, the calvaria RNA contained the messenger for both the α1 and α2 chains of collagen.

Several eukaryotic mRNAs have been translated in heterologous eukaryotic and prokaryotic cell-free systems^{18–26}. This suggests that there are no absolute species-specific or tissue-specific factors required at the translational level of protein synthesis. Our data are further confirmation of this hypothesis.

The molecular sieve chromatography demonstrated the

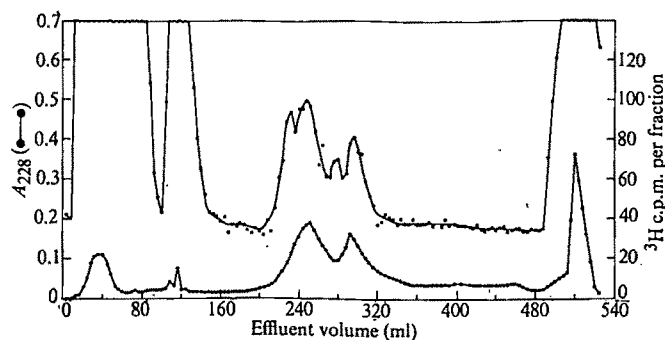


Fig. 2 CM-cellulose chromatography of the *in vitro* synthesised protein. Purified lathyritic chick skin collagen (20 mg) prepared as described previously was added to the dissolved precipitate formed in a large scale reaction (Fig. 1). The sample was heated for 30 min at 40° C and dialysed extensively against 0.04 M Na acetate buffer, pH 4.8 at 4° C. After heating the sample again it was applied to a CM-cellulose column (2.5 × 10 cm) equilibrated with the same buffer and eluted with a 400 linear NaCl gradient from 0.04 to 0.14 M and a final wash with 1 M NaCl in 0.5 M NaOH²⁹. Fractions (4 ml) were collected and the A_{228} and radioactivity of each sample were determined as in Fig. 1: (●) Radioactivity; (○) A_{228} . See Fig. 1 for an explanation of the $\alpha 1$ and $\alpha 2$ terminology.

presence of an *in vitro* synthesised protein as large as authentic chick α chains. The ion exchange chromatography on the CM-cellulose columns provided further evidence that authentic chick collagen had been synthesised. Proteins synthesised in the *in vitro* system co-chromatographed with the $\alpha 1$ and $\alpha 2$ chains of the marker chick collagen.

Pro α chains, the primary product of protein synthesis, have a molecular weight of 115,000⁴ and if present would have eluted from the agarose column at 410 ml. The protein eluting from the CM-cellulose in the region where pro $\alpha 1$ is usually observed just before the $\alpha 1$ carrier^{1,2} was too small to be precipitated in TCA-tannic acid. The pro α chains seem to have been converted to α chains during incubation. Previous studies with the polysome system¹² and with intact calvaria²⁷ indicate rapid and extensive conversion of pro α chains to α chains. The pro α chains may have been degraded through the action of the specific procollagen peptidase¹¹ or a non-specific protease. Either of such activities may be present in the S30 extract.

Table 2 Collagenase Digestion of the *in vitro* Synthesised Protein

Sample	Digestion conditions	TCA-insoluble (c.p.m.)	% protein solubilised
³ H-tryptophan-labelled whole chick extract*	– Collagenase	7,892	<1
	+ Collagenase	7,935	<1
³ H-proline-labelled collagen†	– Collagenase	11,205	<1
	+ Collagenase	450	96
<i>In vitro</i> synthesised protein	– Collagenase	8,830	0
	+ Collagenase	4,027	55

A large reaction (0.2 ml) was prepared and incubated as described in Table 1. Cold proline was added and the sample was incubated for another 20 min. Three aliquots were transferred to glass test tubes for collagenase assay and one aliquot was TCA-precipitated as described in Table 1. Calcium chloride, *p*-ethylmalamide and collagenase³¹ were added to the first sample, only CaCl₂ and *n*-ethylmalamide to the second, and no addition was made to the third. The tubes were all incubated in a shaking water bath at 37° C for 20 min. These samples were then precipitated with TCA-tannic acid. * 5 μ Ci of neutralised ³H-tryptophan were layered on the allantoic membrane of 8-d chick embryos. The chicks were killed after 2.5 h of incubation, the heads were removed and the body doused in phosphate buffered saline. The homogenate was centrifuged at 17,500g for 30 min and stored at –20° C.

† ³H-proline labelled collagen was a gift from Dr David Rowe.

From the data presented here, we conclude that we have identified mRNA activities from embryonic chick calvaria which direct the synthesis of the $\alpha 1$ and the $\alpha 2$ chains of collagen. The mRNAs are functional in an heterologous cell-free system derived from Krebs II ascites cells. The cell-free synthesising system is totally dependent on the addition of mRNA and can be manipulated to be also tRNA dependent. The collagen mRNA is now being characterised, and the role of tRNA in its translational control is being pursued.

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Production by Stimulated Macrophages of Factors depressing Lymphocyte Transformation

MACROPHAGES can inhibit the responses of lymphocytes to a variety of stimuli. The presence of excessive numbers of normal macrophages led to inhibition of antibody formation by cultured mouse lymphoid cells¹⁻³. Normal rat spleen cell suspensions responded better to non-specific stimulation by Gram-negative bacterial lipopolysaccharide (endotoxin) after being freed of macrophages, but the response was reduced again by the addition of macrophages⁴. Spleen cells from mice injected with *Corynebacterium parvum*^{5,6} or subjected to a graft-versus-host (GvH) reaction^{6,7} showed decreased antibody formation⁷ and decreased responsiveness to phytohaemagglutinin (PHA) or allogeneic lymphocytes⁸ when cultured *in vitro*. Such mice possess activated macrophages^{8,9}. Their spleen cell responses were restored, at least in part, by removal of macrophages^{6,7}. Attempts to demonstrate the production of soluble inhibitors by macrophages *in vitro* have generally been unsuccessful^{6,7,10}. Mouse serum can inhibit primary antibody formation¹¹⁻¹⁴ and mitogen-induced transformation of T lymphocytes and B lymphocytes in cultures of mouse spleen cells; we have suggested (ref. 15; D. S. N. and C. N. Shneider, unpublished) that the factor responsible for the latter effect may be produced by macrophages. Here I present evidence that mouse peritoneal macrophages activated *in vivo* produce a potent inhibitor of lymphocyte transformation when cultured *in vitro*.

The mice used were A/J females, CBA/J males and (C57Bl/6J × A/J)F₁(B6AF₁) females. Spleen cells were cultured in triplicate in small flat-bottomed vials as described elsewhere (ref. 15; D. S. N. and C. N. Shneider, unpub-

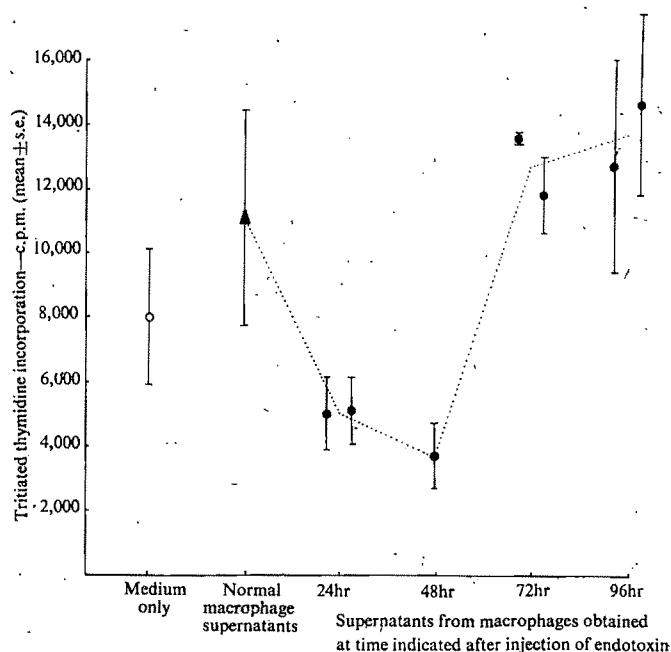


Fig. 1 Effect of supernatants from macrophages of endotoxin-treated CBA/J mice on PHA-induced DNA synthesis by normal CBA/J spleen cells. Donors received 400 µg of *Salmonella typhimurium* endotoxin s.c. at the times shown before collection; this treatment had previously been shown⁹ to produce marked activation. Each point represents the mean of triplicate tests of a single supernatant, except that for normal macrophage supernatants of which five were separate samples each tested in triplicate; the mean value for all five tests is shown. Vertical bars indicate standard errors. The differences between the effects of normal supernatants and those from mice injected 24 or 48 h previously with endotoxin are statistically significant ($P \leq 0.05$).

lished). To 0.6 ml of a suspension containing 7.5×10^6 viable normal spleen cells per ml of medium RPMI 1640 was added 0.4 ml of either RPMI 1640 containing 6.25% heat-inactivated normal human serum ("medium") or the supernatant from macrophages cultured in the same medium. Macrophages were obtained by washing out the peritoneal cavities of mice with 2 ml of Hanks' solution containing heparin (10 U ml⁻¹). Pooled peritoneal washings from three mice ($5-10 \times 10^6$ macrophages) were cultured for 3 h in 35 mm Falcon plastic Petri dishes, in an atmosphere of 5% CO₂ in O₂. The dishes were thoroughly washed with a total of 20 ml RPMI 1640 to remove non-adherent cells. Three ml of the medium was added and the dishes were incubated for 24 h. The supernatants were removed, centrifuged at 750g for 10 min and added to spleen cell cultures either immediately or after storage at -20° C. The mitogens used were: phytohaemagglutinin P (PHA; Difco), Concanavalin A (con A; Calbiochem) and the lipopolysaccharide B (endotoxin) of *Escherichia coli* 055:B5 (Difco). Mixed lymphocyte reactions (MLRs) were induced by mixing 0.3 ml each of A/J and CBA/J spleen cells. Cells were cultured for 48 h or, in the case of MLRs, 96 h. Two µCi of tritiated thymidine (TRA-120, The Radiochemical Centre, Amersham) was added for the last 24 h; the cultures were processed for liquid scintillation counting as described elsewhere¹⁶.

Injection of endotoxins into mice causes morphological and functional activation of macrophages⁸. Figure 1 shows the effect, on PHA-induced transformation of normal CBA/J spleen cells, of culture supernatants from macrophages of CBA/J mice injected with *Salmonella typhimurium* endotoxin. When the mice had been injected 24 h or 48 h before collection of the macrophages the supernatants were markedly inhibitory. Supernatants obtained later were not inhibitory. Supernatants from normal CBA/J macrophages produced a slight but statistically insignificant increase in tritiated thymidine incorporation.

Table 1 Effect of Macrophage Culture Supernatants on PHA-induced DNA Synthesis by Normal A/J Spleen Cells

Material added to cultures	Tritiated thymidine incorporation (mean c.p.m. per culture ± s.e.) in cultures containing:	
	3.1 µg PHA	No PHA
Medium only	17,927 ± 2,880	1,440 ± 88
Supernatant from macrophages of normal mice	13,771 ± 488	2,414 ± 323
Supernatants from macrophages of mice injected 48 h previously with endotoxin from:		
<i>E. coli</i> 055 : B5 (W), 50 µg	7,601 ± 1,302	1,777 ± 144
<i>E. coli</i> 055 : B5 (W), 200 µg	1,718 ± 496	564 ± 78
<i>E. coli</i> 055 : B5 (B), 400 µg	2,621 ± 961	788 ± 110
<i>S. enteritidis</i> (B), 400 µg	2,049 ± 305	446 ± 51
<i>S. typhimurium</i> (B), 400 µg	2,785 ± 394	771 ± 90

Table 2 Effect of Macrophage Culture Supernatants on DNA Synthesis by Normal Spleen Cell Cultures in Response to Different Stimuli

Mouse strain	Stimulus	Tritiated thymidine incorporation in the presence of supernatants of cultures of macrophages from endotoxin-treated mice (% of controls)*
CBA/J	Nil	74
	PHA, 3.1 µg	27
	Con A, 1.2 µg	44
	<i>E. coli</i> endotoxin, 12.5 µg	40
A/J	Nil	49
	CBA/J spleen cells	26

* Macrophage donors injected subcutaneously with 400 µg *S. typhimurium* endotoxin, 48 h previously. Control cultures received medium only instead of macrophage supernatants.

Table 3 Effects of Serum and of Culture Supernatants from Macrophages of Mice with Graft-versus-Host Reactions on PHA-induced DNA Synthesis by Normal B6AF₁ Spleen Cells

Experiment	Material added to cultures	Source of material	Number of samples tested	Tritiated thymidine incorporation (mean c.p.m. per culture $\pm$ s.e.) in the presence of 3.1 μ g PHA
1	Medium only	—	1 (triplicate)	34,940 $\pm$ 2,809
	Medium plus 5% mouse serum	Normal mice	1 (pool from 12 mice tested in triplicate)	4,099 $\pm$ 461 †
	Medium plus 5% mouse serum	Syngeneic controls *	1 (pool from 12 mice tested in triplicate)	4,756 $\pm$ 655 †
	Medium plus 5% mouse serum	Mice with GvHR ‡	1 (pool from 12 mice tested in triplicate)	1,605 $\pm$ 42 §
2	Macrophage supernatants	Normal mice	6 (each tested in triplicate)	25,160 $\pm$ 3,323
	Macrophage supernatants	Mice with GvHR	5 (each tested in triplicate)	12,803 $\pm$ 2 250

* B6AF₁ mice injected with 5×10^7 B6AF₁ spleen cells 11 d earlier.† B6AF₁ mice injected with 5×10^7 A/J spleen cells 11 d earlier.‡ Significantly different from controls containing medium only ($P < 0.01$).§ Significantly different from syngeneic or normal controls ($P < 0.01$).|| Significantly different from cultures containing normal mouse macrophage supernatants ($P < 0.01$).

Table 1 shows the results of an experiment in which supernatants were obtained from macrophages of normal A/J mice, or mice injected 48 h previously with different endotoxins, and added to normal A/J spleen cells, with or without PHA. Supernatants from normal macrophages produced a statistically insignificant depression of PHA-induced DNA synthesis and a significant ($P=0.05$) increase in DNA synthesis in unstimulated cultures. Pronounced and significant ($P \leq 0.01$ in all cases) depression of PHA-induced DNA synthesis was caused by all the supernatants from endotoxin-treated mice; they caused less pronounced depression in unstimulated cultures. In other experiments supernatants taken from 48 h cultures of macrophages (the medium having been changed at 24 h) were much less depressive.

Table 2 summarises the results of two experiments to determine the effect of macrophage supernatants on the responses of normal spleen cells to different mitogens. Supernatants from macrophages of endotoxin-treated mice depressed the responses to all the T-lymphocyte mitogens (PHA, Con A and allogeneic spleen cells in MLRs) and to a B-lymphocyte mitogen (*E. coli* endotoxin).

Mice with GvH reaction were also used to see whether a totally different type of stimulus would increase the depressive activity of mouse serum and induce the production of an inhibitor by macrophages. B6AF₁ mice injected intravenously with 5×10^7 A/J spleen cells were found to undergo a non-fatal GvH reaction, with peak splenomegaly at 10–12 d. In separate experiments, serum and peritoneal macrophages were obtained after 11 d; serum and macrophage supernatants were tested for their effect on PHA-induced transformation of normal B6AF₁ spleen cells. Table 3 shows that, as in other experiments¹⁵, normal serum depressed DNA synthesis. Serum from control mice injected with syngeneic cells was equally depressive, but serum from mice with GvH reaction was markedly and significantly more depressive. Supernatants from macrophages of mice with GvH reaction, compared with control supernatants, also depressed DNA synthesis.

Some implications of these findings may be noted briefly. The production or release by stimulated macrophages of a potent inhibitor of lymphocyte transformation offers an explanation for the inhibitory effect of GvH reaction and *C. parvum* injections on the responses of mouse lymphoid cells to antigens or mitogens⁵⁻⁷. Technical differences may account for the apparent lack of success of other workers^{5,7,10} in demonstrating the existence of soluble inhibitors. It is possible that macrophage-produced factors of this type could play a part in "sequential" antigenic competition, as suggested by Taussig¹⁷, and in the transient but marked depression of antibody formation following endotoxin injections¹⁸. The relationship between macrophage-produced factors and the inhibitor in mouse serum remains to be elucidated, but these findings strengthen the hypothesis¹⁵

that macrophages may be the source of this factor and possibly of the immunoregulatory α -globulin¹⁹ or normal immunosuppressive protein²⁰ found in fractions of normal human plasma, and the depressive factors found in serum from patients with a variety of diseases^{16,21}. Macrophages have now been implicated as a source of soluble factors with a variety of non-specific effects on lymphocyte function including reconstitution of the response of purified lymphocytes in MLRs²²; reconstitution of primary antibody formation by purified lymphocytes²³; potentiation of the response of thymocytes to PHA²⁴; and depression of lymphocyte transformation, as described here. The relationships among the factors responsible remain to be elucidated.

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Sex Ratio in Progeny of Mice Inseminated with Sperm treated with H-Y Antiserum

SPECULATION that immunological means could be used to control the sex ratio in mammals began when Eichwald and Silmsker¹ provided evidence for a Y-linked histocompatibility antigen. Feldman² and Sachs and Heller³ initially suggested that serum from inbred females immunised by skin from males of the same strain (and assumed to contain antibody specifically directed against the Y antigen) might selectively impair the fertilising ability of sperm containing the Y chromosome. Testing of this hypothesis was hampered by lack of adequate systems for demonstrating and assaying H-Y antibody in the sera of immunised females. Consequently experiments designed to examine the possibility of immunoselection of gametes have until now all been carried out *in vivo*, and have involved determining the sex ratio of progeny from female mice that had rejected skin grafts from males of the same strain⁴⁻⁶.

The results of such experiments have been negative or equivocal, but it is not possible to decide whether this is because there is no basis for immunoselection (that is, no preponderance of H-Y antigen on Y-bearing sperm) or because sperm in the female reproductive tract are inaccessible to immunological attack.

We have devised methods for assaying H-Y antibody by the complement-dependent cytotoxicity test on sperm⁷ or on male epidermal cells in suspension⁸. This prompted us to test the effects of artificially inseminating mice with sperm that had been exposed *in vitro* to H-Y antibody of known cytotoxic potency, in the presence of complement. Thus we can re-examine the question of whether there is any expression of genes in post-meiotic cells, which might render Y-bearing sperm more susceptible than X-bearing sperm to cytotoxic H-Y antibody. The data we report here indicate that some degree of immunoselection against Y-bearing sperm is possible.

H-Y antiserum was prepared by grafting C57Bl/6 (B6) females two to eight times with skin from males of the same strain⁷. Serum was collected 6, 8, and 10 d after the second and subsequent skin grafts, and the three bleedings after each graft, from individual females, were pooled and tested for cytotoxic activity on sperm. Sera were used in experiments only when they fulfilled the criterion of killing 20–30% of sperm above controls at a dilution of 1/8 using horse complement⁹. Ninety separately prepared samples of H-Y antiserum were used in this study. For each female to be artificially inseminated pooled epididymal and vas deferens sperm from (B6×A)_F₁ males were mixed with antiserum and complement in these quantities: 5×10⁶ sperm suspended in 0.05 ml undiluted H-Y antiserum plus 0.05 ml absorbed horse serum (complement source) diluted 1/20 in M-199 and incubated 35–45 min at 37° C. About 70–80% of all sperm can be expected to be dead under these conditions; we did not do viability counts on each preparation. The number of sperm used was empirically determined to be the minimum necessary to achieve a satisfactory incidence of fertilisation (5–10% of inseminations resulted in pregnancy); the amount of antibody was limited to 0.05 ml because vaginal instillation of a total volume of more than 0.1 ml is impracticable. The conditions used thus gave the highest feasible antibody:sperm ratios. Recipient females came from random-bred stock, and were inseminated with a 1 ml syringe 24–30 h post-partum, at which time they could be expected to have ovulated¹⁰; post-partum females were chosen because we thought the relaxed condition of their genital tract might favour the retention of the instilled sperm suspension.

Two sets of control data were collected throughout the period occupied by this study. Natural litters born to

random-bred females mated to (B6×A)_F₁ males indicate the normal sex ratio from such males. Second, litters produced by artificial insemination of B6 females with (B6×A)_F₁ sperm treated with anti-H-2^a or anti-H-2^b serum, according to the schedule above, served to control for whether the procedure of artificial insemination itself, or exposure to any mouse antiserum, might adversely affect Y-bearing as compared with X-bearing sperm. [These latter controls incidentally serve as a preliminary test of whether H-2 antigens exhibit "haploid expression", as has been reported for H-LA antigens on human sperm¹¹—but no evidence for haploid expression of H-2 was found, fourteen out of twenty-seven offspring from sperm treated with anti-H-2^a being H-2^a/H-2^b heterozygotes, as were ten out of eighteen offspring from sperm treated with anti-H-2^b.]

Table 1 presents the control data from natural litters at sequential monthly intervals (each of which yields a sample size roughly equivalent to the total progeny obtained from artificial insemination) together with χ^2 and *P* values indicating the deviation of each sample from the overall sex ratio of 53.3% males. No significant departures were found; the individual samples are remarkably free of random variation or seasonal fluctuation.

Table 2 indicates a sex ratio of 45.4% males for progeny of females inseminated with anti-H-Y-treated sperm as compared with 53.4% for natural births and control artificial inseminations combined ($\chi^2=9.7$; *P*<0.003). These results indicate that Y-bearing sperm can be selectively impaired by anti-H-Y antibody; the implication is that sperm containing the Y-chromosome have more H-Y antigen on their surface than do X-bearing sperm, and this in turn implies post-segregational activity of the gene or genes responsible for H-Y antigen. Evidence for low levels of RNA synthesis during spermatid stages in the mouse is given by Monesi¹² and by G. B. Dooher (personal communication).

The simplest interpretation of our data might be that the percentage deviation of the sex ratio observed is a true measure of the average quantitative variance of H-Y antigen between X-bearing and Y-bearing sperm. The relatively minor shift in sex ratio after treatment of sperm with H-Y antibody would on these grounds indicate only relatively small quantitative differences in H-Y between the two types of sperm, implying that much of the sperm membrane is conserved from the diploid state. Immunoelectron microscopy indicates, however, that the representation of H-Y on mouse sperm, in a single sample, ranges from little or none to a certain maximum, with many sperm falling at the two extremes¹³. This may imply that haploid expression is more extensive than the results of this study suggest.

We suspect the immunoselection method we use to be deficient in at least two respects. First, treatment of nucleated cells by antibody and complement in operationally "weak" systems like H-Y invariably leaves many antigen-positive cells viable. Second, H-Y antisera produced by skin

Table 1 Sex Ratios in Monthly Subsamples of Progeny of (B6×A)_F₁ Male Mice

♂	♀	Total	%♂	χ^2	<i>P</i>
146	124	270	54.1	0.06	>0.5
184	153	337	54.6	0.19	>0.5
221	183	404	54.7	0.25	>0.5
343	280	623	55.1	0.64	>0.5
240	215	455	52.7	0.08	>0.5
373	326	699	53.4	0.00	>0.5
272	238	510	53.3	0.00	>0.5
381	329	710	53.7	0.02	>0.5
246	204	450	54.7	0.32	>0.5
235	232	467	50.3	1.68	>0.2
182	185	367	49.6	2.14	>0.1
106	104	210	50.5	0.69	>0.5
196	161	357	54.9	0.28	>0.5
			53.3		

Table 2 Effect of Anti-H-Y Treatment of Sperm on Sex Ratio of Progeny Obtained by Artificial Insemination

a	Controls	♂	♀	% ♂	
Litters after natural matings	3,125	2,734	5,859	53.3	
Litters after anti-H-2 treatment of sperm and artificial insemination	57	41	98	58.2	$\chi^2 = 1.0 \quad P > 0.3$
Totals	3,182	2,775	5,957	53.4	
b Experimental litters after anti-H-Y treatment of sperm and artificial insemination	169	203	372	45.4	$\chi^2 = 9.7 \quad P < 0.003$

grafting are commonly contaminated with non-H-Y antibody that is cytotoxic for sperm. This was fully appreciated only when Koo¹³, studying H-Y antigen on mouse sperm by immuno-electron microscopy, established that epidermal cells and sperm share an autoantigen to which an immune response is provoked by skin grafting¹³. This antibody must to an unknown degree have produced indiscriminate cytolysis of sperm in our experiments, thus lowering the sensitivity of the method.

Satisfactory approaches to remedying both these deficiencies are known, and we are studying them. In the meantime, there is a strong possibility that a more pronounced deviation of the sex ratio than we have yet achieved is attainable in the mouse.

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Induction of Synthesis of Extracellular Cell-wall Degrading Enzymes in Vascular Wilt Fungi

THE vascular wilt fungi *Verticillium albo-atrum* and *Fusarium oxysporum* f. sp. *lycopersici*, pathogenic to tomato plants, are characteristically confined to the vascular

elements where they produce substances causing disease symptoms. The identity of these substances is still controversial. Both fungi, however, readily produce *in vitro* enzymes that degrade various polysaccharide components of plant cell walls and there is evidence that one or more of these enzymes may be implicated in the wilt syndrome. Information already available on enzyme synthesis is contradictory, and so information on factors controlling synthesis of these enzymes may, therefore, contribute to understanding of pathogenesis in vascular wilts.

As some of the past work on synthesis was based on methods now known to be unsatisfactory in certain respects, we have re-investigated the problem with techniques that avoid difficulties inherent in much of the earlier work. These difficulties are overcome by limiting the availability of the substrate in a continuous-feeding culture, thus reversing the effects of catabolite repression operative in batch culture containing excess substrate. This approach has been effectively used by other workers to reveal the true nature of inducibility of polysaccharide-degrading enzymes¹⁻³. We describe here a more rapid and highly reproducible technique applicable to shake-flask cultures.

The fungi were grown on a medium containing inorganic salts (N as NaNO₃) and the following carbon sources: various sugars and uronides found as constituents of plant cell wall polymers; polymers containing linkages found in herbaceous cell walls including sodium polypectate, pectin, carboxymethyl cellulose, xylan, arabinan and cell walls prepared from stems and petioles of 7-week-old tomato plants, grown at 25° C, by the method of Karr *et al.*⁴

Standardised inocula of fungal spores were obtained by transferring 1 ml of a sucrose (1.5%)/salts culture of *V. albo-atrum*, or sucrose (1.5%)/casamino acids culture of *F. oxysporum* grown for 3 d on a rotary shaker (150 r.p.m.) at 25° C into 50 ml glucose (0.5%)/salts shake culture; after 40 h cells, mainly as conidia and bud cells, were collected by centrifugation and suspended in 100 ml inorganic salts medium contained in 250 ml Erlenmeyer flasks at 150 r.p.m. Little or no glucose was carried over with the cells.

Various carbon sources were supplied to shake cultures from diffusion capsules⁵ from which they passed into the ambient liquid at low linear rates determined by their concentration and number of membranes through which they diffused (restricted cultures). Capsules were replaced before sugar release became non-linear. For most purposes 100 ml cultures were supplied at the rate of 2-4 mg sugar h⁻¹. For comparison carbon sources were added directly to the medium at initial concentrations of 1% (w/v) (unrestricted cultures); insoluble compounds were added as finely divided powders.

At intervals after inoculation shake cultures were assayed for growth and, after dialysis, for one of a number of enzyme activities on the polymers listed above and galactan (from the lupin), and also for β -D-galactosidase, β -D-mannosidase, β -D-glucosidase, β -D-glucuronidase and α -L-fucosidase activities against their respective *p*-nitrophenol derivatives. Enzyme activities were measured as release of reducing sugars⁶ (arabinanase, xylanase and galactanase), saturated and unsaturated galacturonides by a modified thiobarbituric acid test⁷, endo-polygalacturonase (endo-PG) and endo-pectin *trans*-eliminase (endo-PTE), *p*-nitrophenol (aryl glycosidases), and by viscometric assay (endo-PG and cellulase (Cx)). All activities are corrected for fungal growth by expressing enzyme units per 4×10^8 spores ml⁻¹.

In cultures of *V. albo-atrum* on cell walls, a number of cell wall degrading enzymes were produced sequentially during the growth period of 2-9 d. Endo-PG was synthesised after 2 d followed by arabinanase and endo-PTE. Xylanase and cellulase (Cx) activities were detectable at very low levels before 6 d after which production was rapid. β -D-Galactosidase activity and low levels of β -D-glucosidase activity were also detected. Sequential polysaccharide synthesis has been reported for other plant pathogenic fungi grown on host

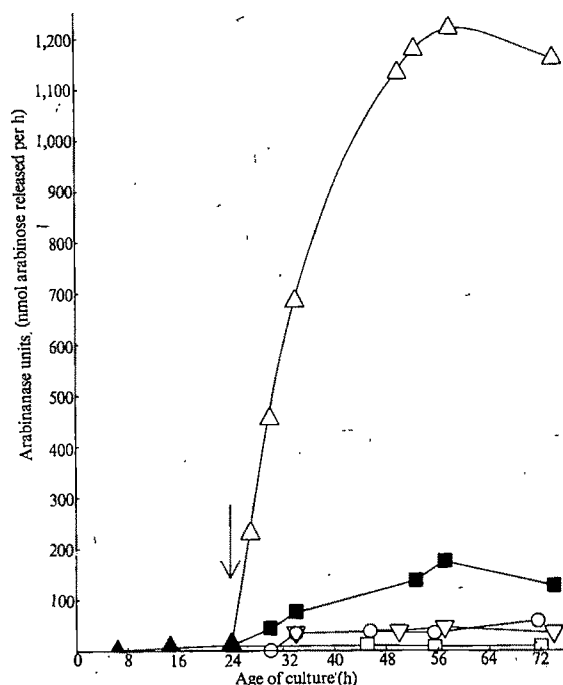


Fig. 1 Induced and constitutive synthesis of arabinanase by *V. albo-atrum*. Sugars were supplied in excess in unrestricted (U) cultures or at 2–4 mg per 100 ml per h in restricted (R) cultures. ▲—▲, Glucose (R); △—△, arabinose (R); ○—○, arabinose (U); ▽—▽, xylose (R); □—□, xylose (U); ■—■, galactose (R). Other cell-wall sugars allowed constitutive synthesis of the same order or below that of xylose (R) and have been omitted for the sake of clarity. The arrow depicts the time when diffusion capsules containing sugars to be screened for their ability to induce enzyme synthesis replaced capsules from the 24 h glucose pretreatment.

plant cell walls⁹; in each case a similar sequence was observed. There were no significant differences in enzyme activities of filtrates from *V. albo-atrum* cultures on cell walls from resistant and susceptible host plants. Specific activities were generally much higher than in cultures grown on solutions of particular polymers. *F. oxysporum* cultures were not analysed in the same detail, but after 11 d high activities of a similar range of polysaccharidases to those produced by *V. albo-atrum* were detected.

Unrestricted cultures gave results that were difficult to interpret in terms of induction and repression of enzyme synthesis as, indeed, is much of the published work. Polysaccharidase activities were generally absent or very low in these conditions. More easily interpreted results were obtained from restricted cultures in which the concentrations of sugar monomers in the culture fluid remained between 0 and 0.001% (w/v) during growth of the pathogen. In these conditions the growth rates of *V. albo-atrum* and *F. oxysporum* (measured as spore number h⁻¹) were respectively 1/11–1/30 and 1/8.5 of those in unrestricted culture.

If enzyme synthesis is constitutive and controlled by catabolite repression, then one or more of the enzymes mentioned above should accumulate in cultures with a restricted supply of glucose^{1,2}. In cultures grown for 48 h at pH 3.5, 5.5 and 7.5, however, activities of each enzyme were either absent or barely detectable.

In further experiments in which various monomeric sugars were tested as inducers of enzyme synthesis, cultures of the pathogens were pretreated with restricted glucose-feeding for 24 h to decrease the steady-state concentration of intracellular metabolic intermediates, because the response of microorganisms in a repressed state to the presence of inducers is less rapid. Capsules containing glucose were then replaced with others containing various sugars. Periodic assays of dialysed culture filtrates showed that almost always

enzyme synthesis was specifically induced as follows: endo-PG and endo-PTE by D-galacturonic acid, arabinanase by L-arabinose, xylanase by D-xylose, galactanase and β -galactosidase by D-galactose, and cellulase (Cx) by cellobiose. A characteristic pattern of induced and constitutive enzyme synthesis is given by arabinanase (Fig. 1).

An interesting anomaly was that for synthesis of galactanase and β -galactosidase, L-arabinose was a much more effective inducer than D-galactose. This enhanced synthesis was approximately four times greater for *F. oxysporum* β -galactosidase and seven to ten times greater for *V. albo-atrum* β -galactosidase production on restricted arabinose compared with restricted galactose cultures. In the early stages of induction, however, the maximum rate of synthesis was achieved by *V. albo-atrum* on arabinose after only 2.5 h; at this stage enzyme activity was sixty-fold greater than in comparable galactose cultures. A similar degree of cross-induction by galactose on arabinanase synthesis also occurs. The highly specific induction of synthesis of other enzymes by both pathogens was also very rapid. Thus, for *V. albo-atrum* after 3 h, xylanase and arabinanase activity had reached one third and one fifth respectively of the maximum specific activities detected after 36 h growth. No α -D-mannosidase, α -L-fucosidase, β -D-glucuronidase or β -D-xylosidase activities were detected in any culture conditions.

The degree of specificity of induction of synthesis by *V. albo-atrum* is shown in Table 1. Similar results were obtained for *F. oxysporum*. Specificity was virtually complete for endo-PG, endo-PTE and cellulase (Cx). It was high for the other enzymes and probably higher than indicated because of the difficulty in distinguishing between constitutive synthesis and apparent constitutive synthesis arising from the action of enzymes on a heterogeneous substrate such as arabinan containing some galacturonic acid. Thus, the arabinanase apparently synthesised in response to galacturonic acid may reflect the activity of endo-PG or endo-PTE on regions of the arabinan polymer containing galacturonic acid. Where the substrate is pure or the enzyme assay is definitive, however, induction of synthesis is highly specific.

The above results suggested that even in conditions of induction by particular sugars, synthesis could be affected by catabolite repression if the concentration of the monomer in culture became excessive. Accordingly, *V. albo-atrum* was supplied with various monomeric sugars at different rates, and cultures were assayed for enzyme activity per unit of fungal growth. Synthesis of endo-PG and endo-PTE increased almost linearly when supplied with galacturonic acid

Table 1 Induction of Synthesis of Polysaccharidases of *Vorticillium albo-atrum* by a Restricted Supply of Cell-wall Sugars

Inducer†	Enzyme activities*					
	Endo-PG	Endo-PTE	Arabinanase	β -Galactosidase	Xylanase	Cellulase (Cx)
D-Galacturonic acid	100	100	15.8	0	16.5	0.30
L-Arabinose	0	0	100	100	3.5	0.25
D-Galactose	0	0	14.4	12.9	5.2	0.37
D-Xylose	0	0	3.7	0.26	100	0.08
D-Glucose	0–1.25	0	0–5.8	0.34	5.8	1.46
D-Mannose	0	0	0	0.34	0	0.20
L-Rhamnose	2.10	9.11	6.6	0	0	0.40
L-Fucose	1.38	0.16	0	0	0	0.25
Cellobiose	3.7	1.34	—	0	—	100
D-Glucuronic acid	—	—	—	—	—	—

* Enzyme activities are expressed as a percentage of the maximum specific activities attained in culture after identical periods of exposure to different sugars.

† Sugars were fed from diffusion capsules at linear rates of 2–4 mg per 100 ml per h to shake cultures of *V. albo-atrum* containing initially 4×10^9 spores ml⁻¹.

* D-Glucuronic acid is not utilised by this strain of *V. albo-atrum*.

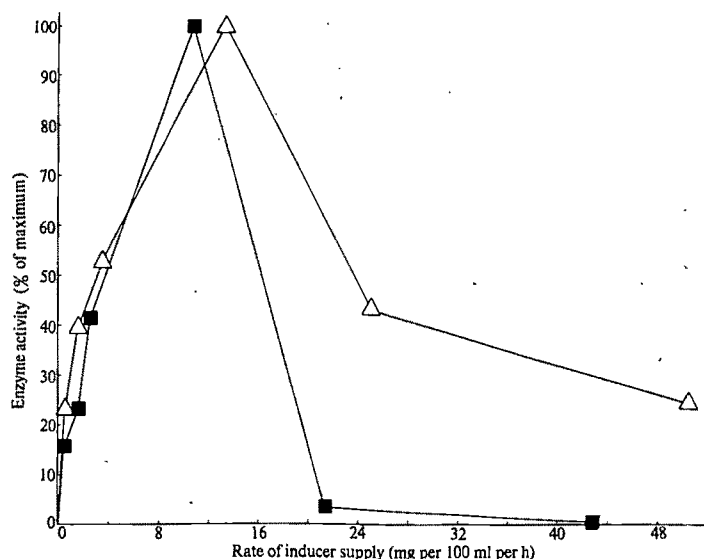


Fig. 2 Synthesis of endo-PG (■—■) and arabinanase (△—△) by *V. albo-atrum* in restricted cultures supplied with increasing rates of galacturonic acid and arabinose respectively. Enzyme activities are expressed as percentages of the maximum specific activity attained 10 h after addition of inducer.

from 0 to about 10 mg per 100 ml per h but decreased rapidly at higher values, for example about 90% at 20 mg per 100 ml per h. At twice this rate, repression of synthesis was almost complete. Synthesis of arabinanase and B-galactosidase on arabinose followed a similar pattern up to the same optimum rate of inducer supply beyond which synthesis continued at the relatively high rates of 22–67% of the maximum even at rates of about 50 mg per 100 ml per h and greater (Fig. 2). Further analysis showed that when enzyme synthesis started to decrease, inducing sugars began to accumulate in the cultures.

These results emphasise the highly inductive nature of synthesis of a variety of enzymes that degrade polymers of plant cell walls, especially those acting on pectic substrates, and the extreme susceptibility of this synthesis to catabolite repression. The results for the pectic enzymes are of particular interest because of the evidence that implicates them in the wilt syndrome. Their synthesis is induced in a highly specific manner by galacturonic acid, constitutive synthesis is at very low rates and synthesis is very sensitive to catabolite repression. The induction of enzyme synthesis by pectic polymers probably depends on the release of galacturonic acid by constitutive enzyme; once the process is initiated it should become autocatalytic. *Prima facie*, conditions in vascular elements would seem to be suitable for the synthesis of these enzymes and in this connection we have isolated from stems of tomato plants infected with *V. albo-atrum* amounts of an endo-pectin trans-eliminase which are of the same order as those which when applied to healthy cuttings reproduce many of the natural symptoms of a vascular wilt.

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Ethylene as a Cause of Soil Fungistasis

SOIL fungistasis is the term applied to the widespread inhibition of the germination of fungal propagules in soil under apparently favourable conditions unless supplied with exogenous nutrient¹. No satisfactory explanation has been given for this phenomenon although a number of hypotheses have been proposed².

Experiments in our laboratory with water-saturated airstreams passing over soil implicated a volatile factor as the cause of soil fungistasis. Volatile inhibitors are assuming increased importance as possible causes of fungistasis^{2,3} since Balis and Kouyeas⁴ suggested that a volatile unsaturated hydrocarbon may be involved. Volatile materials were identified by gas chromatography from about fifty soils collected throughout Australia with different origins and histories. Ethylene was the only material identified in all soils in concentrations likely to be biologically active. Ethylene has recently been identified in soil under anaerobic conditions⁵. In this study, ethylene was found to be produced in appreciable quantities in open, aerobic systems. Results with sterilised soil indicate that the ethylene is formed by microbial activity.

Soils to be tested for production of volatiles were dried for 24 h at 40° C and passed through a 0.1 cm mesh sieve; 30 g samples were packed into glass tubes (16 cm by 2.5 cm) and wetted to field capacity. Gas samples were withdrawn from a 3.5 ml sampling tube fitted into the base of each soil tube. Ethylene was identified by flame ionisation chromatography using a stainless steel column packed with Poropak N. Identification was confirmed against authentic samples of ethylene on 0.35 m and 2.0 m Poropak N columns and by the use of the mercuric perchlorate technique⁶.

Ethylene production and chemical properties of some of the soils studied are given in Fig. 1 and Table 1. There is a correlation between organic matter and total nitrogen content of soil and ability to produce ethylene.

Sclerotia of *Sclerotium rolfsii* Sacc. and spores of *Helminthosporium sativum* Pamm., King and Bakke were used in experiments to determine if a relationship exists between the ability of a soil to produce ethylene and its level of fungistasis. The soils cited in Table 1 were dried and sieved as described; 20 g samples were placed in Petri dishes of diameter 9 cm and wetted to field capacity. Filter paper wicks dipping in water maintained the soils at field capacity. With *S. rolfsii*, thirty mature sclerotia taken directly from potato dextrose agar (PDA) cultures were placed on the soil surface in each Petri dish. One Petri dish of each soil was left on the laboratory bench where air turbulence caused by air-conditioning units was measured to be 13–17 m min⁻¹ (non-aerated treatment). In a duplicate sample of each soil a water-saturated airstream (150 ml per min per dish) was passed through a hole in the centre of the Petri dish lid so that the air flowed over the surface of the soil and out at the edge of the lid. Germination of sclerotia in aerated and non-aerated treatments is shown in Fig. 2 and Table 2. Germination of spores of *H. sativum* was similarly tested, mature spores being collected from a spore suspension on filters of diameter 4.7 cm and pore size 0.22 µm: the filters were placed on the soil surface in the centre of each Petri dish, and germination of spores was recorded on aerated and non-aerated soil (Table 3).

These experiments confirm that there is a correlation between the ability of a soil to produce ethylene and its level

Table 1 Chemical Analyses of Soils

Soil	Origin	pH	Organic matter %	Total N %	PO ₄	Ca	Mg	Na	K
Kidd from avocado grove, South Queensland	Basalt	5.8	25.1	0.67	4.9	22.9	6.0	0.8	0.47
Mt Wilson from grassland, New South Wales	Basalt	5.6	13.1	0.36	0.7	6.8	1.6	0.9	0.21
Ashburner from avocado grove, South Queensland	Basalt	6.6	14.3	0.62	4.9	21.2	5.1	0.2	1.74
Duranbah from avocado grove, north New South Wales	Basalt	4.9	9.4	0.40	3.2	1.9	0.7	2.3	0.37
Mullumbimby from avocado grove, north New South Wales	Basalt	6.4	18.7	0.32	140.7	13.4	4.8	0.1	1.01
Gosnell from <i>Eucalyptus marginata</i> forest, Western Australia	Lateritic sand	5.2	4.8	0.02	0.7	0.8	0.2	0.1	0.04
Penrith from garden soil, New South Wales	Alluvial	5.8	3.8	0.18	164.6	8.6	2.2	0.4	1.18
Rydalmere from potting loam, New South Wales	Alluvial	5.8	6.4	0.11	4.3	5.7	2.2	0.3	0.39
Epping from garden soil, New South Wales	Shale	5.8	5.7	0.15	116.4	8.1	1.2	0.3	0.32

Table 2 Germination (%) of *Sclerotium rolfsii* Sclerotia on Non-aerated and Aerated Soil

Soil	Non-aerated		Aerated (150 ml min ⁻¹)	
	3 d	6 d	3 d	6 d
Kidd	0	17	20	73
Mt Wilson	7	20	17	43
Ashburner	3	23	13	60
Duranbah	7	23	23	47
Mullumbimby	17	30	17	53
Gosnell	0	23	53	77
Penrith	23	50	60	83
Rydalmere	7	40	20	83
Epping	13	43	47	67

of fungistasis. The few anomalies in the results are to be expected because of interaction of other factors such as differences in microbial competition and levels of nutrient in the soils. The results clearly show the nullifying effect of an airstream on fungistasis.

To establish that ethylene causes fungistasis, a series of glass tubes (16 cm by 1.3 cm) containing a layer of either Ashburner or Penrith soils (5 g dry soil per tube) were prepared, soil

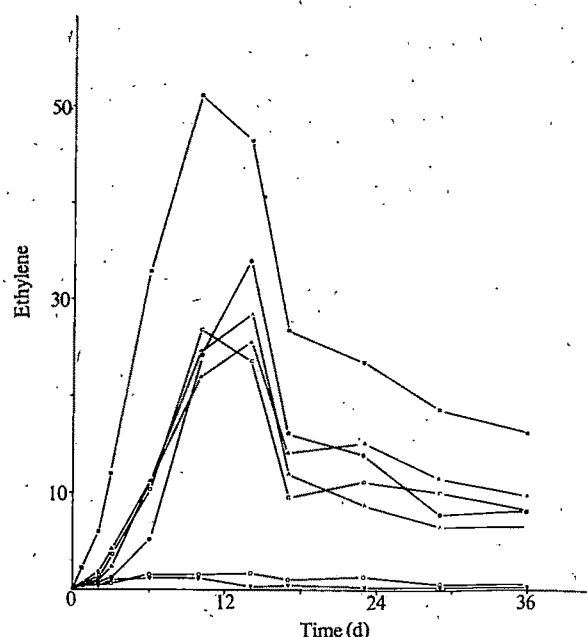


Fig. 1 Ethylene production by soil. Rydalmere and Epping soils produced ethylene at levels between those produced by Gosnell and Penrith soils but their curves are omitted from the graph to avoid confusion. Soils: ■, Kidd; ▲, Mt Wilson; □, Ashburner; ●, Duranbah; △, Mullumbimby; ○, Gosnell; ▼, Penrith.

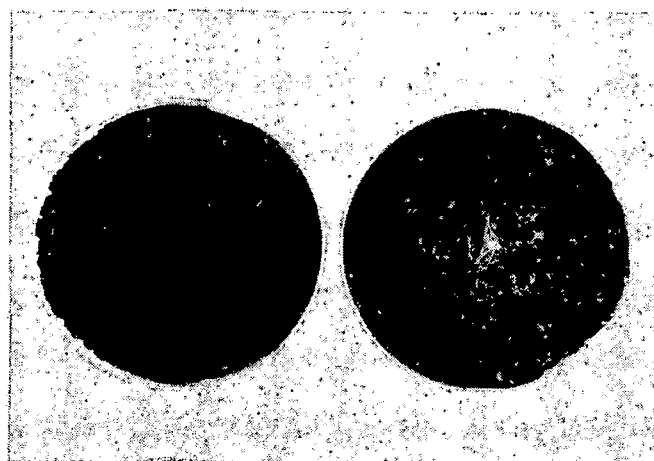


Fig. 2 Germination of sclerotia of *Sclerotium rolfsii* on Rydalmere soil. Left, non-aerated; right, aerated with airstream through hole in centre of Petri dish lid.

was wetted to field capacity, and sclerotia of *S. rolfsii* placed on the soil surface. Three treatments were used with each soil: a saturated airstream (500 ml min⁻¹) containing less than 0.01 volumes per million (v.p.m.) ethylene, a saturated airstream (500 ml min⁻¹) containing 1 v.p.m. ethylene passed over the soil, and a still atmosphere maintained in tubes by plugging their ends with cotton wool. Germination of sclerotia is shown in Table 4.

Moulds proliferated to form a dense mycelium on the soil surface in all tubes treated with an airstream without ethylene. No mould growth was visible in other treatments. Fungi isolated from the mycelia on the soil surface included species of *Pythium*, *Fusarium*, *Trichoderma*, *Penicillium*, *Aspergillus*, *Cephalosporium*-like fungus, and many unidentified fungi. Germination of the test fungus was relatively poor in the presence of vigorous mould growth and this may result from

Table 3 Germination* (%) of *Helminthosporium sativum* Spores† on Non-aerated and Aerated Soil

Soil	Non-aerated	Aerated (150 ml min ⁻¹)
Kidd	4	61
Mt Wilson	9	63
Ashburner	4	51
Duranbah	7	52
Mullumbimby	5	36
Gosnell	13	67
Penrith	19	65
Rydalmere	8	67
Epping	7	60

* After 3 d.

† At least 400 spores counted per treatment.

competition. At the end of the experiment, a water-saturated airstream without ethylene was passed over sclerotia inhibited from germination in both non-aerated and ethylene-treated tubes. Many sclerotia then germinated within a few days and moulds developed on the soil surface. Thus, at the levels tested, ethylene causes no permanent damage to sclerotia of *S. rolfsii* or to the mould propagules.

Table 4 Effect of Ethylene on Germination (%) of *Sclerotium rolfsii* Sclerotia on Soil

Soil	Aerated + (v.p.m. C_2H_4) (500 ml min ⁻¹)	Aerated (500 ml min ⁻¹)	Non-aerated
Ashburner	0	35	0
Penrith	0	48	10*

* Only sclerotia nearest ends of tubes germinated.

Although all soils tested were fungistatic, they showed marked differences in ability to produce ethylene. Evidence from other experiments with addition of organic amendments to soil shows that there is an interaction between nutrient levels for microbial growth and the concentration of ethylene required to maintain fungistasis. Soils rich in nutrients produce more ethylene but such soils require higher levels of ethylene to inhibit germination of fungal propagules. Thus, following the terminology of Watson and Ford², nutrient is the main stimulator of propagule germination and ethylene the main inhibitor. The balance between the two determines whether a soil is fungistatic at any given time. This balance between stimulator and inhibitor would also explain why the addition of nutrients to soil temporarily annuls fungistasis¹.

Ethylene also affects other microorganisms including bacteria, actinomycetes and nematodes in soil and, therefore, will almost certainly have a marked influence on most soil processes including turnover of organic matter and mineralisation of nitrogen. The concept of a balance between nutrient, the stimulator, and ethylene, the inhibitor, has far-reaching implications for the study of the occurrence and control of soil-borne plant diseases, especially those caused by fungal pathogens.

Chemical analyses of soils were done by the Chemistry Branch, Biological and Chemical Research Institute, Rydalmere.

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of energy whereas subsequent hops could rely extensively on elastic rebound. If this were the case, then the kangaroo's unusual saltatory mode of locomotion should be an energetically inexpensive way to move.

Recent studies on quadrupedal mammals have shown that the energetic cost of their locomotion varies in a regular manner with size, and the oxygen consumption of a running mammal can be predicted quite closely if its speed and weight are known¹. This relationship between weight and energetic cost of locomotion for quadrupedal animals provides a baseline against which the energy expended by the hopping kangaroo can be compared. In this study we set out to answer the simple question: Is it cheaper for an animal to hop or to run?

Two red kangaroos (*Megaleia rufa*, 18 and 28 kg average weight, both female) were trained to hop on a treadmill (236 cm long and 76 cm wide) while wearing a lightweight ventilated face mask. Steady state oxygen consumption was measured for 5 to 20 min while they travelled at speeds from 1.0 to 22 km h⁻¹. Air temperature was 24° C and wind speed was approximately matched to tread speed. Oxygen consumption increased to a nearly constant value after a minute of hopping at each speed and returned to the resting level almost immediately after the animal stopped. We assumed that the constant level reflected a steady state oxygen consumption and that there was no significant anaerobic metabolism since the oxygen debt observed after a run never amounted to more than 2% of the oxygen consumed during the run. Furthermore, it was clear that maximum levels of aerobic metabolism had not been reached during our experiments, for when the animal struggled we observed oxygen consumption values up to twice those observed at the highest speeds at which we were able to achieve sustained hopping. Oxygen consumption of the animal was measured by pulling room air through a mask at metered rates (300 to 340 l min⁻¹) and measuring the difference in oxygen concentration between air entering and leaving the mask (using a Beckman F-3 paramagnetic oxygen analyser). The error involved in this procedure was determined to be less than ±2% by bleeding nitrogen into the mask at known rates (simulating the extraction of oxygen by the animal). In separate experiments stride frequencies were counted at speeds from 1.0 to 25 km h⁻¹. Each reported observation is the mean of three half-minute counts. Stride length was calculated from stride frequency and treadmill speed.

At low speeds the kangaroo does not hop but moves by what can perhaps best be described as a 'pentapedal type' of locomotion, since the animal uses its heavy tail as a fifth leg. This type of locomotion has also been called 'slow progression'². When moving in this manner the animal (starting with its hind feet and tail on the ground): (a) puts its front feet on the ground and pulls its tail towards the body causing the hind limbs to lift until only the rear toes are touching; (b) swings its hind limbs forward together while supporting itself on its front limbs and tail; (c) lifts its front legs off the ground; and (d) moves its front feet forward as it repeats the cycle. This form of locomotion not only looks awkward but appears to be energetically quite costly compared to quadrupedal running (Fig. 1a). Oxygen consumption increased nearly linearly as the animal increased its speed from 1 to 6 km h⁻¹ while moving pentapedally (slope 0.66; y intercept 0.35; correlation coefficient 0.96 for the 18 kg animal). Oxygen consumption at 6 km h⁻¹ was about twenty times the predicted standard metabolic rate³. The observed slope for the relationship between oxygen consumption and pentapedal speed was 3.9 times that predicted for an 18 kg animal running on four legs. The increase in speed while moving pentapedally was achieved primarily by increasing stride frequency (Fig. 1b) and stride length increased only slightly (Fig. 1c).

The kangaroos changed from the 'pentapedal type' of locomotion to bipedal hopping between 6 and 7 km h⁻¹. As the animals increased their hopping speed (from 7 to 22 km h⁻¹ in the smaller kangaroo) there was a slight decline in oxygen consumption. This slight decline does not represent a maximum

Energetic Cost of Locomotion in Kangaroos

THE hopping of kangaroos is reminiscent of a bouncing ball or the action of a pogo stick. This suggests a significant storage and recovery of energy in elastic elements. One might surmise that the kangaroo's first hop would require a large amount

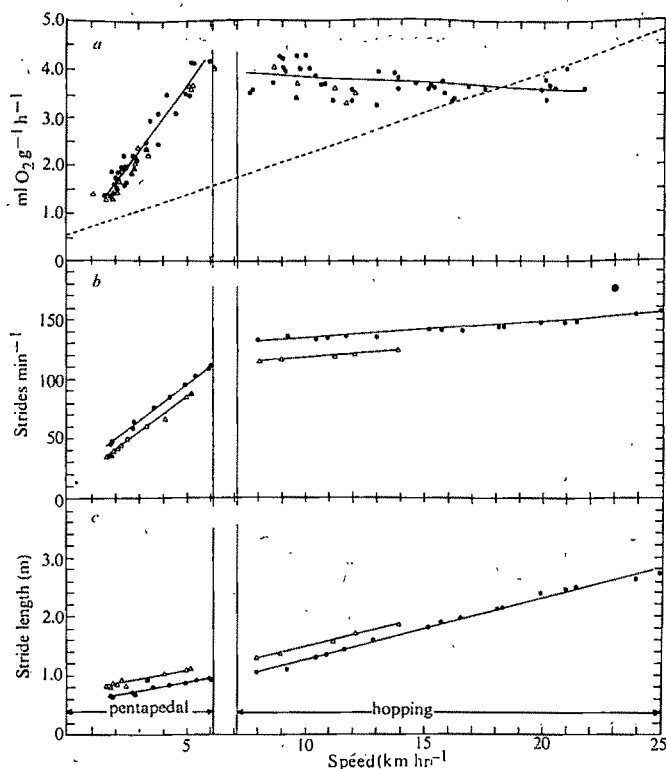


Fig. 1 *a*, Steady state oxygen consumption; *b*, stride frequency; *c*, stride length of the red kangaroo as a function of speed. The dashed line in *a* represents the oxygen consumption predicted for an 18 kg mammal running quadrupedally¹. Data are from two female animals which weighed 18 kg (●) and 28 kg (Δ). The regression lines for oxygen consumption as a function of speed were calculated (method of least squares) using only the data from the 18 kg animal. For pentapedal locomotion, $n=27$, slope=0.66, y intercept=0.35, correlation coefficient=+0.96 $P<0.001$. For hopping, $n=39$, slope=-0.026, y intercept=4.09, correlation coefficient=-0.40 $P<0.01$. Stride frequency was measured separately from oxygen consumption, thus the data points in *b* and *c* do not correspond with those in *a*. The lines for stride frequency and stride length as a function of speed were fitted by eye.

sustained oxygen consumption since the animals were capable of more than doubling their metabolism above this level when they struggled. The values for oxygen consumption of the 28 kg kangaroo tended to be lower than those from the 18 kg animal (Fig. 1*a*). We were, however, unable to obtain higher speeds safely with the larger animal because our treadmill was too short.

The number of hops min^{-1} , like the oxygen consumption, was nearly the same over a wide range of speeds (Fig. 1*b*), thus the animals increased their speed primarily by increasing the distance per hop (Fig. 1*c*). The almost constant hopping frequency observed over a three-fold change in speed means that the duration of each hop is constant. The time on the ground, however, decreases and time off the ground increases. The 18 kg kangaroo with its shorter legs hopped at a higher frequency than the 28 kg animal.

Although the distance per hop increased with increasing speed, the amount of energy expended per hop was nearly constant. Thus the animals achieved greater acceleration on take-off as they moved faster, without expending more energy. This is probably due to a greater storage and recovery of energy in the elastic elements as the animals travel at higher speeds.

The tendons and ligaments in the rear limbs and the tail seem admirably suited for storage of elastic energy. The achilles tendon is an extremely large tendon (approximately 1.5 cm in diameter and 35 cm in length in a 40 kg animal which we dissected). Badoux⁴ comments that the very long calcaneus seems to act as a lever for the tendons and ligaments of the

more force would be applied on this lever causing greater stretching of these elastic elements. Recovery of this stored energy on take-off might well explain the slight decline in oxygen consumption with increasing speed of hopping. It is also possible that other systems play a role in elastic storage of energy as the kangaroo hops, and the classic example of the suspensory or springing ligaments of the horse fetlock comes to mind⁵. Two broad sheets of tendons run along both the ventro-lateral and dorso-lateral aspects of the tail. The ventral tendons appear involved in pulling the tail towards the animal during pentapedal locomotion while the dorsal ones might be involved in elastic storage of energy during hopping.

From our data it is seen that at speeds of less than 18 km h^{-1} the hopping kangaroo expends more energy than a running four-legged animal of the same weight, but at speeds exceeding 18 km h^{-1} it appears to be cheaper to hop. Accurate measurements of speeds at which undisturbed kangaroos ordinarily travel in nature are not available. Kangaroos can, however, travel at speeds considerably faster than the maximum speeds which were possible in our studies. Most observers agree that large kangaroos can sustain speeds of 40 km h^{-1} for several km and may reach 50–65 km h^{-1} in short bursts^{2,6}.

It is difficult to understand why large hopping herbivores are found only in Australia, since hopping appears to be such an inexpensive way to travel at high speeds. The energetics of hopping, however, may give some insight into the survival of the large hopping herbivores of Australia while their quadrupedal counterparts became extinct. Some 20,000 to 30,000 yr ago, before Palaeolithic man arrived in Australia, the marsupial fauna was much more diverse than at present. There were predators such as the marsupial lions (*Thylacoleo carnifex*) and Tasmanian wolves (*Thylacinus cynocephalus*). There were also large quadrupedal herbivores, some of which were the size of a rhinoceros, for example *Diprotodon* sp. One might speculate that the kangaroos were able to sustain higher speeds when being pursued than those other large terrestrial marsupials, as a result of the low energetic cost of hopping. This could explain how they survived the introduction of man and his dog, the dingo, while the large quadrupedal marsupials became extinct.

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Reference Abbreviations

ALL abbreviations of references in *Nature* should now conform to the style of the *World List of Scientific Periodicals*, fourth ed. (Butterworth, 1963–65). Authors submitting manuscripts are asked to ensure that the references are written appropriately.

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BOOK REVIEWS

After Kinsey

The Female Orgasm: Psychology, Physiology, Fantasy. By Seymour Fisher. Pp. x+544. (Allen Lane: London, April 1973.) £5.

PROFESSOR FISHER'S book, which deals primarily with the psychology, fantasy and partly with the physiology of the female orgasm, is complementary to the earlier works of Masters and Johnson^{1,2} and Kinsey^{3,4}. Although a significant book by any standards it is not as innovative as its predecessors. The first one-third of the book is divided into five chapters which comprehensively review a commendably large and diverse selection of the literature on the "female sexual response". This is a valuable source of reference for the many workers, medical and non-medical, working in the field.

The remaining ten chapters of the volume contain data that Professor Fisher accumulated prospectively on some two hundred and eighty female volunteers recruited as seven samples. To satisfy different criteria they were studied over differing lengths of time and with somewhat differing procedures. In summary, however, virtually all were subjected to interviews galore, a battery of standard psychological tests, numerous self-rating questionnaires and in most cases physiological measurements, including galvanic skin response (finger, breast, labia, ankle), temperature, heart rate and so on. The sheer volume of data collected was enormous by any standards and allowed diverse statistical analyses.

I am sure Professor Fisher will not take issue with me if I say that the majority of his findings, which are negative correlations, provide more questions than answers, although in general the data accord well with Kinsey's earlier sociological information and the more recent physiological correlates of Masters and Johnson^{1,2}.

What, then, are Fisher's positive findings? Perhaps the most important, since it tends to contradict Masters's insistence of the pre-eminence of the quality of physical stimulation in orgasmic response in the female, is that "a feeling of emotional security and of being loved were more important to the female than were stimulative techniques, prowess of the male, length of foreplay, variation in coital positions, frequency of coitus, and so on". Fisher speculates that this might have psychological roots in childhood when a "demanding and definite (as contrasted with a

casual and permissive) father" made an immutable (sexual) impact. (An implicit plea for an increase in parental discipline?) Unfortunately, Fisher's boldness deserts him less than half a page further on when, winding up the discussion on the genesis of sexual responsiveness, he states "because of the imperfect techniques available for measuring the variables involved, one cannot begin to define realistically how influential these early (parental) transactions are. They could be enormously important and even the prime determinant of orgasmic potential". He clearly believes this even if he does not assert it. In common with those from more recent contributors, Fisher's data surely destroy the old but pernicious psychoanalytical chestnut that vaginal orgasm is better and more mature than clitoral orgasm, which was represented as being neurotic. Fisher provides abundant psychometric data which indicate unequivocally that mental health is not associated either with the "allegedly" differing types of orgasm, or indeed with sexual responsiveness at all. This must be somewhat of a kick in the teeth for the classical psychoanalyst who, in spite of all, continues to maintain that clitoral orgasm is infantile and frigidity is sick.

The book concludes with some practical implications, sub-sectioned under the headings "Pathways to Sexual Adequacy", "Sex Education", "Sexual Adequacy", "Sex and Mental Health", "Treatment of Orgasm Difficulties", "Non Sexual Functions of Sex", "Education", "Sexual Practice Affects"; and pregnancy and priority problems in the study of female sexuality.

A. J. COOPER

¹ Masters, W. H., and Johnson, V. E., *Human Sexual Response* (Little Brown, Boston, 1966).

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Calorific Homeostasis

Regulation in Metabolism. By E. A. Newsholme and C. Start. Pp. xiii+349. (Wiley: New York and London, April 1973.) £6.

THE ability of an organism to adjust selectively the chemical processes taking place in some of its cells in response to the environmental change is of great fascination. This book describes how

the activities of certain enzymes associated with the provision of fuel for oxidation are controlled, or in the words of the authors' preface, the maintenance of "calorific homeostasis". The scope is therefore limited to control of carbohydrate and fat metabolism in, for the most part, mammalian tissues. Control of amino acid, nucleotide and amine metabolism is excluded, as is the role of protein biosynthesis and degradation in those pathways which are covered in this book and the title *Regulation in Metabolism* is thus possibly misleading. One can, however, appreciate the authors' dilemma in attempting to produce a book which deals in depth with the mechanisms by which certain enzymes and hence pathways may be controlled, whilst keeping the scale, and hence price, down sufficiently for students to be able to afford to buy it. A soft-back version would surely be welcome.

The first two chapters cover the theoretical basis of regulation of enzyme activity and metabolite levels (allostery, substrate cycling, enzyme interconversions) and the identification of control points in a pathway. The remaining five chapters deal in detail with the control of carbohydrate metabolism in muscle and liver, and control of fat metabolism in liver and adipose tissue. Although the factual content is high, the text is very readable with a liberal use of tables and diagrams, and more than 400 references are cited. The complexities of intermediary metabolism often bewilder the student but Newsholme and Start have successfully integrated not only those parts of carbohydrate and fat metabolism which overlap, but also some areas of physiology and biochemistry. For example the control during starvation of plasma glucose and fatty acid levels is explained in terms of the action of ketone bodies on (i) lipolysis in adipose tissue, (ii) glucose oxidation in brain and muscle, and (iii) release of insulin from the pancreas. A useful final section covers many of the known biochemical effects of a restricted number of hormones (insulin, growth hormone, adrenaline and glucagon). It would also have been useful if the same treatment had been given to cyclic AMP.

Errors are few and mostly trivial, although the suggestions that (i) the result of donkey spleen deoxycytidine monophosphate deaminase action on dCMP is dAMP, and (ii) valine and isoleucine are degraded to glutamate, should have been spotted. It is also misleading of the authors to state that fatty acid oxidation is the only

physically organised pathway, when recent research is revealing the existence of multi-enzyme complexes containing many or most enzyme activities associated with specific biochemical pathways.

Generally, however, the book is highly recommendable to any undergraduate (or graduate) biology student who has received a basic biochemistry course. It can only serve to increase the student's interest in the mechanisms of biological regulation.

A. R. HIPKISS

Immune Responsiveness

Genetic Control of Immune Responsiveness: Relationship to Disease Susceptibility. Edited by Hugh O. McDevitt and Maurice Landy. (Proceedings of an International Conference held at Brook Lodge, Augusta, Michigan, May 8-10, 1972.) Pp. xviii+469. (Academic: New York and London, April 1973.) \$19.50.

THIS handy book presents the well planned, three-day discussion on the genetic control of immune responsiveness which took place at Brook Lodge in May 1972. It is well designed, and excellently edited by H. O. McDevitt and M. Landy. The book does more than document the symposium; it gives a systematic and comprehensive survey of the genetics of immune responses, different aspects of which are treated precisely by scientists, eminently competent in their respective fields, whose names are often synonyms for their work. The discussions themselves do not simply paraphrase the material presented, but elaborate new views. The book avoids the common tedium of conference reports, and can serve as a text and reference book, both of which are lacking in this area. In this context, however, references to original papers would be desirable.

The six chapters (followed by an extensive commentary by M. Cohn) deal with histocompatibility-linked Ir genes, the H-2 region, Ir genes linked to allotypes, T and B cell receptors, control of disease susceptibility and HL-A type and disease. This classification is practical and also delineates principal aspects of genetic control of immune responsiveness as we see them today.

Immune response (Ir) genes are distinguished genetically and functionally as histocompatibility and as immunoglobulin-heavy chain allotype-linked genes. Several models of genetic control cannot, however, yet be classified (Sela, Biozzi). The histocompatibility-linked Ir genes are interpreted as dealing with the specific recognition of antigens by T cells or even determining the T cell receptor itself (Benacerraf, McDevitt). This concept, of course, leads to an extensive discussion of the nature of the

T cell receptor: immunoglobulin *pro* and *con* (Unanue, Uhr, Warner). The question remained open.

The major histocompatibility systems of mouse (H-2) and man (HL-A) are introduced by Shreffler and Cèppellini, respectively. As illustrated by F. Bach and van Rood, serologically defined H antigens are distinct from other functions of these gene regions; that is, MLC (mixed lymphocyte culture) stimulation, graft rejection, genetic control of immune response. Some examples of allotype linked control presumably reflect presence or absence of the respective structural genes (v genes) for receptors on B lymphocytes (Cohn, Nisonoff). But other types might represent still unknown mechanisms (for example, monoclonal antibodies, Krause).

The concept of Ir genes has important theoretical and medical implications. It might be the key to a new analytical approach to studying susceptibility to infectious, autoimmune and neoplastic diseases, at least as far as immune reactions are involved. Lilly gives an example of how multigenic control already can be analysed (Friend virus disease). It is further shown that genetically controlled immune responses can either prevent or cause virus disease (Oldstone). In man, only studies on the population level of associations between HL-A system and disease are reported (Bodmer). Family studies, such as Levine's on pollen allergy, are not yet included in this book.

Bodmer presents a stimulating genetic model for major histocompatibility systems: that is, large clusters of related genes, which presumably arose by evolutionary gene duplications and which control functions such as graft rejection, MLC stimulation, disease susceptibility, antigen recognition and serologically detectable H antigens. Associations at the population level then reflect linkage disequilibria between closely linked genes.

M. Cohn systematically summarises the theoretical implications of genetic control of immune responsiveness and their bearing on generation of diversity and self-tolerance in terms of his theory of associative recognition. This is literally a purgatorium of all facts and ideas presented before. Cohn makes explicit (and the book implicit) that facts must be separated from contaminating tacit assumptions and also that they become meaningful only within a conceptual framework, which prevents them from becoming misleading.

The reader, overwhelmed by data and interpretations, may be consoled by a sentence (easily generalised) from F. Bach: "Who isn't confused about MLC isn't thinking clearly" (he might even become proud of it).

F. GÖTTMANN

Electrochemistry

Electrochemical Systems. By John S. Newman. Pp. xiv+432. (Prentice-Hall: Englewood Cliffs, New Jersey, January 1973.) \$18.95.

READING this book emphasises the range of the study of electrochemistry and the possibility of creating interest by the nature of the attitude adopted to create coherence in the subject.

The approach is predominantly that of the chemical engineer; illuminating at times but rather insensitive in those areas where the chemistry of the materials could be involved as a major interest, and with an indifference to techniques of experimentation. The result is an interesting and in some ways quite a valuable book; a good companion to more conventional texts and certainly, and of course deliberately, more comprehensive in coverage than is customary. Thermodynamics, electrode kinetics, electrokinetics, ionic transport processes, current distribution and mass transfer are treated.

The author is happiest in his exposition of phenomena which may be described and satisfactorily handled by a formal treatment; essentially areas, as defined by the author on page 1 of the book, where electrochemistry may be regarded as macroscopic science in the absence of a need for correlation with microscopic or molecular concepts. This is strongly to be contrasted with the approach to electrochemistry as followed by some more chemically oriented authors, in which the interest is essentially atomistic and preoccupied by adsorption and electron transfer; these are difficult electrochemical problems, germane to a full understanding of the interfacial processes but, no matter how complex the treatment, not yet yielding to a theoretical approach.

Many practising electrochemists will read the contents of this book relating to the handling of the macroscopic aspects of the subject with interest and benefit; the chemical engineer, diverting his thoughts to electrochemistry, in particular should become happier in certain aspects of the application of his professional skills. It would be kind, however, to omit comment on the chapter on electrode kinetics, a section most necessary to such a continued education.

A feature of the book and one according to the American pattern is the rather extensive lists of examples at the end of each major section. I regard them with mixed feelings. It is a respected pedagogic procedure to provide students with such exercises but the value is purely much diminished in the omission of answers and even some guidance to the solution of some of the questions. Some, too, refer to un-

one would have thought, applied scientists should be taught to avoid.

In all, a useful book bringing a refreshing, if formal, approach to a number of problems.

H. R. THIRSK

Dividing and Developing

The Cell Cycle in Development and Differentiation. Edited by M. Balls and F. S. Billett. Pp. xi+483. (Cambridge University: London, May 1973.) £11.

THIS volume contains twenty-six papers concerned with some biological aspects of cell division and the cell cycle in plants, protozoa, and some species of multicellular animals. The editors state in their preface that the book is intended to complement that of Mitchison (*The Biology of the Cell Cycle*, Cambridge University Press, London, 1971) which summarises what is known of the cell cycle in prokaryotes as well as in synchronous cell populations of eukaryotes and of vertebrates *in vitro*.

There are two general reasons why a knowledge of the cell cycle may be important in the study of cell differentiation. One is that there are cyclic variations in some kinds of nuclear or gene activity, and these are related to stages of the cell cycle. Cyclic variations of this kind have been clearly established for DNA synthesis, histone synthesis, and certain kinds of enzyme activity. It is clear, however, that there is not yet sufficient information to say whether gene activity is in general regulated in this cyclic way. In view of the recent development of sensitive methods of determining the amounts of newly synthesised messenger RNAs of known kinds, it should now be possible to determine for several different genes whether their expression fluctuates consistently within a cell cycle, either at the level of transcription, translation, or post-translational modification. Until much more information of this kind is available it is hard to plan clear-cut experiments designed to analyse the relationship of the cell cycle to gene expression in molecular terms.

The other interesting question relating the cell cycle and cell differentiation concerns the possibility of a connection between a certain phase of the cell cycle such as mitosis or DNA synthesis and the induction of new gene expression. Many authors have suggested within the last 10 years that cells must pass through a phase of DNA synthesis or a mitosis, between the time when a cell is acted upon by an inducer of differentiation (such as erythropoietin) and the time of realisation of that differentiation (in this case haemoglobin synthesis). If true, this relationship could be of great importance in understanding cell differentiation. At present, however, there is no

experimental system which is ideally suited to the investigation of this question. In this symposium only the paper of Harrison *et al.* is concerned directly with this potentially important matter.

In view of the lack of information about changes in gene activity during the cell cycle, it is not surprising to find that most contributors have given what amounts to a descriptive account of variations in the frequency or duration of a cell cycle in the developing system of their choice. These include Bennett (plant meiosis), Barlow (plant root meristem), Lynden (plant shoot apex), Biggelaar (mollusc development), Rudkin (insect polytene chromosomes), Chibon (newt embryos), Graham (early mouse development), and Steel (cultured human cells).

Some other contributors have described patterns of RNA synthesis or of enzyme activities which are characteristic of tissues composed of cells mostly at a known stage of the cell cycle. Examples of papers in this category are those of John *et al.* (*Chlorella*), Grant (*Physarum*), Yeoman and Aitchison (cultured plant cells) and Giudice (sea urchin oocytes).

Only a very few authors have attempted a truly experimental analysis of factors which cause cyclic changes in nuclear or gene activity. A shining example of this is the elegant work of Ord, involving nuclear transfers in *Amoeba*. In addition Grant describes attempts to obtain changes in the activity of isolated nuclei.

The volume ends with a few very useful summaries of subjects which are of topical, though sometimes controversial, interest: for example, Harrison *et al.* and Cole and Tarbutt (erythropoiesis), Hardy and Ling (mitotic activation of mammalian lymphocytes), Harris and Olsen (metabolic DNA), and Rytömaa (chalones).

It is principally the thorough review articles with an ample supply of references which justify publication of symposia such as the one under review. Apart from containing a number of such articles, this symposium succeeds well in bringing together work on a wide range of eukaryote organisms. I think it will form a useful addition to the library of those interested in the cell cycle and in some aspects of development.

J. B. GURDON

Rat Adenohypophysis

Ultrastructure of Rat Adenohypophysis: Correlation with Function. By Allen Costoff. Pp. xiii+220. (Academic: New York and London, February 1973.) \$14.50.

THE twelve chapters in this book, in addition to an introduction, describe the experimental procedures used by the

author; the several types of glandular cells of the pars distalis (a chapter being allocated to each); the pars tuberalis; the pars intermedia; the biochemical properties of isolated granules and the morphological aspects of the secretory process. Extensive bibliographies are provided at the end of each chapter and there are many electron micrographs of varying quality.

It is obviously difficult to write a book of this type; and, in this instance, because of the rigid subdivision of the topics the work lacks coherence. A final chapter giving a critical appraisal of the significance of the numerous observations referred to in the text would have been of great value. The lack of such a critical assessment is, to my mind, a serious defect in a book which, although it provides much information, fails adequately to emphasise what is significant or, indeed, acceptable. An example of this is to be found in the chapter on the adrenocorticotrophic cell, where in the same section, having stated that certain Japanese workers had reported the dimensions of the secretory granules to be about 200 μm in diameter, the author (from his own observations) reports them to be about 106 μm . This discrepancy passes without comment and one therefore wonders whether, in fact, the same kind of cell is being described.

Finally, very little indeed is said about the ultrastructure of the non-glandular components of the pars distalis—interstitial (stellate) cells, the connective tissue and its associated cells, the blood vessels and their perivascular spaces, and basement membranes. These topics do not appear in the index.

In summary, this book is a compilation of observations unaccompanied by any serious attempt at evaluation.

C. L. FOSTER

Radiation

Radiation Chemistry. By A. J. Swallow. Pp. xi+275. (Longman: London, January 1973.) £5.50.

THIS book aims to provide an overall picture of the whole field of radiation chemistry, and is intended not only for radiation chemists but also for readers whose main interests lie in subjects related to radiation chemistry, ranging from nuclear technology and radiation physics through photochemistry and chemical kinetics to polymer science and radiation biology. The encompassing of such a broad field is a considerable task, and the author has kept the length of the book within bounds by the expedient of discussing illustrative examples of typical work rather than presenting a detailed survey of each topic. Thus the book is aimed at the beginner rather than the expert.

The author begins with a short account of natural and artificial sources of radiation, which includes brief descriptions of the working principles of nuclear reactors, X-ray machines and particle accelerators. Next come chapters on the absorption of radiation in matter and on dosimetry. Chapter 4 is a description of the manner in which the primary species of excited molecules, electrons, positive ions and free radicals are produced as a result of radiation absorption by matter, and of the extent and importance of their roles in the ensuing processes. Brief descriptions of the methods by which such short lived intermediates are observed include electron spin resonance spectroscopy, mass spectrometry and pulse radiolysis. This chapter lays the foundation for the succeeding chapters which deal with the particular systems of inorganic solids, gases, water and aqueous solutions, organic compounds, polymeric systems and substances of biological interest. These topics reflect the broad scope of the book, which should give newcomers to radiation chemistry a good introduction to the whole range of the subject, as well as provide radiation chemists with useful starting points in areas outside their specialised fields of research.

The book is produced in an easy style with good use of footnotes and cross referencing in the text. Selected references to other works are given at the end of each chapter, and there is a good subject index and a useful appendix of units and conversion factors. The author has set a number of problems, with answers, at the end of each chapter which should aid the reader in his understanding of the subject. The book is well illustrated, and there are several quite extensive tables of data on such quantities as bond energies, proton and electron affinities and rate constants which would seem more appropriate to a reference work.

On the whole this is a book to be recommended and it should find a place in most science libraries.

G. V. BUXTON

Quantitative Materials

Problems in Materials Science, Vol. 1. Edited by H. D. Merchant. Pp. x+476. (Gordon and Breach: New York, London and Paris, 1972.) £12.30.

ONE of the interpenetrating pecking orders that bedevil life in universities is the hard science/soft science hierarchy. Ever since Lord Kelvin uttered his memorable chestnut about the impossibility of knowing anything properly unless one can measure it, the applied mathematicians and their imitators have played upon the inferiority complexes of the botanists, mineralogists, zoologists, metallurgists and many others. Each of the sciences has become pro-

gressively more quantitative, and this is a natural and inevitable progression. What can be seriously misleading is the suggestion that close observation, pattern perception, the recognition of correlation between events (whether or not correlation coefficients are estimated) are no part of the stuff of science but rather a kind of pre-scientific pap. The quantitative approach is central to science and has been at least since the time of Tycho Brahe, but so is the skill of the close observer. Tycho Brahe and Johannes Kepler are coupled in scientific history.

This slightly exaggerated outburst is prompted by contemplation of the volume under review. The editor complains that metallurgy or materials science is apt to be taught in a qualitative manner, and to counteract this he intends the book as "an aid to solving problems". Individual authors deal with fields such as diffraction, diffusion, nucleation and growth, thermodynamics, interfaces, magnetic fields, mechanical testing. Each chapter has an introduction which is essentially a minitext on quantitative aspects of the field, then some problems are solved *in extenso*, finally a number of bare problems are added, without solutions.

Certainly a skilled university teacher can mine this quarry and find a number of helpful problems to illustrate his own systematic teaching, though it must be said that for this purpose a complete set of model answers would have been distinctly helpful. But it is hard to see how a student (final-year undergraduate or first-year graduate, at whom the book is aimed) could possibly hope to cope with more than a modest fraction of the (mostly) very advanced subject matter. Complicated tensor treatment of crystal elasticity jostles with first-principle estimates of elastic moduli of various rubbers, the Boltzmann transport equation and its implications, and the advanced treatment of thermal vibrations. No undergraduate I have ever encountered in the materials field could (or should be expected to) cope with some of this subject matter, though other parts, such as Tegart's treatment of mechanical testing or Nussbaum's of magnetic fields, should be more readily accessible.

The impulse which led to the writing of this book is entirely understandable, but the consequent search for particularly quantitative fields has led to a choice of topics and a level of treatment which are generally more appropriate to a graduate theoretical physics course. This is not materials science, but parts of the book (rather less than half, probably) can be used by an experienced teacher in the field as useful source material. The book cannot be recommended for self-study.

The names of two of the contributors

(McLean and Tegart) are misspelled and the page numbers in the table of contents are incorrect.

R. W. CAHN

Canadian Fish

Pacific Fishes of Canada. (Bulletin 180: Fisheries Research Board of Canada, Ottawa.) By J. L. Hart. Pp. ix+740. (Information Canada: Ottawa, 1973.) \$8.

THE study of the fish fauna of the North Pacific commenced with the explorations of the Imperial Russian expeditions of the early nineteenth century, and while some of the fishes described, such as the salmon, *Oncorhynchus* spp., occur on the Canadian Pacific coast, knowledge of that fauna was sparse until almost the present century. Such descriptions as existed were the result of British surveying expeditions, and later of the work of the early school of American ichthyologists, notably D. S. Jordan and C. H. Gilbert.

This history resulted in the literature on Canadian Pacific fishes being scattered through numerous sources until 1946 when Clemmens and Wilby published the first faunistic treatment of the region. The publication of their *Fishes of the Pacific Coast of Canada* stimulated further research and a second, revised edition appeared in 1961. The present volume by J. L. Hart, although ostensibly a lineal descendant of Clemmens and Wilby's book, is an original work and a totally new synthesis of the literature. The contents are organised systematically, each species is well illustrated with new and excellent drawings, and major headings include a description, life history, and distribution. The description is the conventional listing of body proportions but has subsections for meristic data for fin elements and scales, as well as colour notes. A most helpful innovation is the separate heading "Recognition" where characteristic features are itemised. Dichotomous keys to families or orders are clearly set out with quite unambiguous couplets and there are general keys to the classes of fish treated.

Up to date faunistic treatments are of fundamental importance and, with this new work, the Canadian fish fauna is one of the most competently and exhaustively treated. Hart's book will be of great value to fishery workers and students of other disciplines, for it is a modern synthesis of high standard. The author is to be congratulated on the conciseness and clarity of presentation of his material, and the editorial staff of the Fisheries Research Board of Canada deserve commendation for their foresight in commissioning such a fundamental work and for producing it at a very reasonable price.

ALWYN WHEELER

TELEVISION REVIEW

Black Holes— Authorised Version

QUICK on the heels of October's *Horizon* programme about black holes, the BBC last week presented *Not Seeing Is Believing*, a fifty-minute lecture about black holes by Dennis Sciama of Oxford University. The *Horizon* programme (see *Nature*, **245**, 467; 1973) should really have been billed as a programme about gravity in general. Black holes were not mentioned until near the end, when the presenter, John Taylor of King's College, London, was seen draped over flagstones bordering the ornamental pond at Herstmonceux, uttering profound thoughts about black holes in this Universe being white holes in the next, and so on.

Anyone left mystified by John Taylor (and there must have been many) should have turned to Dennis Sciama for a clear account of the basics—what black holes are, why astronomers think black holes should exist, how we might look for them, and their generally-agreed properties. But it was strictly for *aficionados* of astronomy; right at the beginning we had supernovae, radio galaxies, and quasars, without any definitions at all, and soon we were onto event horizons and the language of the astrophysicist.

On top of that there is the difficulty of turning a lecture into good television. Sciama was speaking before an audience of students at St Andrews University—not in an intimate lecture theatre, like the cosy one at the Royal Institution in London that has often been used by the BBC, but in one of those places with a long demonstration bench in front of an array of blackboards.

This problem was overcome by illustrating the lecture with animated drawings projected onto a huge screen above the speaker. These moving drawings were accompanied by a recorded commentary by Dr Sciama, in a more tranquil tone than his lecture theatre voice, that nicely broke up the forceful delivery of the rest of the lecture. The animated drawings—actually not much more complicated than blackboard sketches—themselves contributed a lot to the programme. We saw matter being swept into black holes, gravitational waves being emitted as a star collapsed, and two black holes coalescing, each developing a proboscis like a Gerald Scarfe cartoon of Edward Heath's nose. It was a neat way of coping with the lecture format, and the white drawings on the black background of the screen seemed particularly appropriate for theoretical astrophysics.

The programme was altogether a very creditable performance. It was presented by the Open University in conjunction with the Royal Astronomical Society, and shown during the Open University's television time. It is, however, very much the kind of programme that graduates of Patrick Moore's late-night astronomy programme would appreciate.

It is also good to see the Royal Astronomical Society taking a part in bringing the excitement of modern astronomy before the public. The society has recently become interested in astronomy education, and this lecture is meant to be the first of a series of public expositions on modern developments in astronomy, the society suggesting the topic, supplying the speaker, and paying his fee. The Royal Astronomical Society is perhaps the most entrancing of the scientific societies in London, even allowing for the transfer of its meetings from its own lecture room in Burlington House to the more cosy but less magical Scientific Societies Lecture Theatre in Saville Row; it has an enthralling history, and its members are carrying out some of the most exciting research work that is going on today. The society ought to be better known to the public.

EDWARD PHILLIPS

CORRESPONDENCE

Open Journal

SIR,—May I suggest for *Nature* a radical, healthy change in what I regard as an essentially ailing magazine (not a journal, while present policies persist)? You say (*Nature*, **244**, 475; 1973) "*Nature* must be an open journal, reflecting the sense of community which is very strong among scientists." If you mean what you say, my advice is that you should sign your editorials, strip the sobriquets from your coyly labelled "Cell Biology Correspondent", etc., and publish a masthead. Then we can start talking about an open journal.

The snide sharpshooting from behind shields of anonymity, which has become so characteristic of *Nature* that it is now known in many circles as *Ill-Nature*, is, I am convinced, a direct result of a smug journalistic tradition of anonymity which is totally out of place in a scientific publication and which other scientific journals have long abandoned. Do you in fact stand

behind your own "fine words"? Are you a man, a mouse, or a gnome? How can we tell, when you don't even tell us your name? Are we mortals who have names to conclude you're God? Or that you think you are? Do you dare to print this letter? At least you know who it comes from, since I am not afraid to sign myself

F. PETER WOODFORD

1 Akenside Road,
London NW3 5BS

Nature will have a masthead in January. Full biographical details appeared earlier this year (**243**, 110; 1973) from which readers may care to deduce more about my personality. They may also assume that I write the leaders in constructing their identikit of me.—ED.

Arginine Deficiency

SIR,—In the background information to the discussion on orotic aciduria and arginine deficiency, Milner and Visek

stated¹ that Scull and Rose had shown² that "the growing rat . . . requires arginine for optimum nitrogen retention and normal growth." In point of fact, Scull and Rose had concluded³ that arginine was not required by the rat. The initial data on the essential nature of arginine were based on studies with chicks³.

Yours faithfully,

A. ARNOLD

Reinsselaer, New York

¹ Milner, J. A., and Visek, W. J., *Nature*, **245**, 211 (1973).

² Scull, C. W., and Rose, W. C., *J. biol. Chem.*, **89**, 109 (1930).

³ Arnold, A., Kline, O. L., Elvehjem, C. A., and Hart, E. B., *J. biol. Chem.*, **116**, 699 (1936).

A list of books received will appear in the January 4 issue of *Nature*.

Announcements

University News

Professor Edward Parkes has been appointed Vice Chancellor of the City University to succeed Sir James Tait.

Dr B. J. Aylett has been appointed Professor of Chemistry at Westfield College, University of London.

Dr M. Sandler has been appointed Professor of Chemical Pathology at the Institute of Obstetrics and Gynaecology, University of London.

Dr T. A. Sears has been appointed Professor of Neurophysiology at the Institute of Neurology, University of London.

Dr R. L. Smith has been appointed Professor of Biochemical Pharmacology at St Mary's Hospital Medical School.

Professor J. P. Quilliam has been elected Chairman of Convocation of the University of London to succeed Sir Charles Harris.

Dr John Knott, University of Cambridge, and Dr Richard Dolby, The Welding Institute, have been awarded the 1973 L. B. Pfeil Prize of the Iron and Steel Institute and the Institute of Metals.

Miscellaneous

The following have been awarded The National Medal of Science of the United States: Daniel I. Arnon (University of California); Carl Djerassi (Stanford University); Harold E. Edgerton (MIT); William Maurice Ewing (Marine Biomedical Institute, University of Texas); Arie Jan Haagen-Smit (California Institute of Technology); Vladimir Haensel (Uni-

versal Oil Products Company); Frederick Seitz (The Rockefeller University); Earl W. Sutherland, Jr. (University of Miami); John Wilder Tukey (Bell Laboratories and Princeton University); Richard T. Whitcomb (NASA) and Robert Rathbun Wilson (National Accelerator Laboratory).

Professor David T. Griggs of the University of California at Los Angeles has been awarded the Arthur L. Day Medal of the Geological Society of America.

Dr M. King Hubbert of Stanford University has been awarded the Penrose Medal of the Geological Society of America.

The Gas Chromatography Discussion Group is no longer associated with the Institute of Petroleum and is now called the Chromatography Discussion Group.

International Meetings

December 10, New Polymers from Silicate Materials (The Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1X 8PS).

December 12-13, Symposium on the Humber Estuary (Dr N. V. Jones, Department of Zoology, The University of Hull, Hull HU6 7RX).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

The British Non-Ferrous Metals Research Association. Annual Report for 1972. Pp. 48. (London: The British Non-Ferrous Metals Research Association, 1973.) [117]

World List of Films on Bees and Beekeeping. Provision edition. Pp. vii+67. (London: Bee Research Association, 1973. Obtainable from Bee Research Association, Hill House, Chalfont St. Peter, Gerrards Cross, Bucks.) 50p; \$1.50. [117]

Scientific Instrument Manufacturers' Association of Great Britain. 56th Annual Report, 1972/1973. Pp. 22. (London: Scientific Instrument Manufacturers' Association of Great Britain; 20 Peel Street, W8, 1973.) [127]

Sampling in the Mineral and Metallurgical Processing Industries. (Papers presented at a meeting held in London on 2 July 1973.) Pp. 65. (London: The Institution of Mining and Metallurgy, 44 Portland Place, W1, 1973.) £5. [127]

Central Statistical Office. Research and Development Expenditure. (Studies in Official Statistics No. 21.) Pp. 136. (London: HMSO, 1973.) £1.55 net. [127]

Forestry Commission. The Marketing of Forest Tree Seed and Plants within the European Economic Community. Pp. 8. *Gratis*. Leaflet No. 55: Hydratongs. By F. B. W. Platt and P. Wood. Pp. 10. 10p net. Leaflet No. 56: Grey Squirrel Control. By Judith J. Rowe. Pp. 17. 12p net. Leaflet No. 57: Replacement of Elm in the Countryside. By A. F. Mitchell. Pp. 4. 4p. Research and Development Papers. No. 94: Cablecrane Design Studies. By D. Biggs. Pp. iii+52. No. 95: Some Aspects of Recreation Planning in the Forestry Commission. By A. J. Grayson, R. M. Sidaway and F. P. Thompson. Pp. 16. No. 96: Construction and Application of Stand Yield Models. By G. J. Hamilton and J. M. Christie. Pp. 14. No. 97: Report of a Working Party on Lorry Transport of Roundwood. By P. C. Ormrod and P. C. Stern. Pp. 22. Forest Commission Library Review, No. 25, April 1973. Pp. i+28. (London: Forestry Commission, 1973.) [127]

Other Countries

US Department of the Interior: Geological Survey. Bulletin 1332-D: Lithologic Characteristics of Pliocene Rocks Cored at Elk Hills, Kern County, California. By William M. Berryman. Pp. iii+56+plate 1. (Washington, DC: Government Printing Office, 1973.) [187]

Smithsonian Contributions to Zoology, No. 144: The Behavior of Ocellated Antbirds. By Edwin O. Willis. Pp. 57. (Washington, DC: Smithsonian Institution Press, 1973. For sale by US Government Printing Office.) 90 cents. [187]

Gesellschaft für Strahlen- und Umweltforschung MBH, München. Jahresbericht 1972. Pp. 229. (München: Gesellschaft für Strahlen- und Umweltforschung MBH, 1973.) [207]

National Research Council of Canada. Report of the President, 1972/1973. Pp. 121. (Ottawa: National Research Council of Canada, 1973.) [207]

The Year Book of the International Council of Scientific Unions, 1973. Pp. 135. (Paris: International Council of Scientific Unions, 1973.) [207]

Publications du Centre National pour l'Exploitation des Océans. Série: Rapports Scientifiques et Techniques. No. 15: L'Élevage de la Seriole au Japon. Par A. Muller-Feuga. Pp. 53. (Paris: Centre National pour l'Exploitation des Océans, 1973.) [207]

CERN—European Organization for Nuclear Research. CERN 73-7: Étude d'Un Détecteur pour des Particules de Hautes Énergies—La Chambre à Projection Tridimensionnelle. Par A. Breskin. Pp. vi+135. (Geneve: CERN, 1973.) [237]

United States Department of the Interior: Geological Survey. Professional Paper 646-C: Gravity, Magnetics, and Geology of the San Andreas Fault Area, Near Cholame, California. By W. F. Hanna, S. H. Burch and T. W. Dibble, Jr. Pp. iii+29+4 plates. (Washington, DC: Government Printing Office, 1972.) [237]

The Geological Society of America. Publications Catalog 1973/74. Pp. 83. (Boulder, Colorado: The Geological Society of America, 1973.) [237]

Centre National pour l'Exploitation des Océans. Rapport Annuel 1972. Pp. 80. (Paris: Centre National pour l'Exploitation des Océans, 1973.) [237]

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APPOINTMENTS VACANT**IMPERIAL COLLEGE****Department of Chemical Engineering and Chemical Technology**

Applications are invited for the appointment of a POSTDOCTORAL RESEARCH ASSISTANT to study RADIATION CHEMISTRY OF OSMOTIC MEMBRANE MATERIALS under the supervision of Dr P. G. Clay.

Applicants should be experienced in the use of radiation and in the relevant fields. The appointment is tenable for 2 years and the salary scale is £1,929 to £2,058, plus £162 London Allowance (with F.S.S.U. benefits).

A curriculum vitae and the names of two referees should be sent to Professor G. N. Walton, Dept. of Chemical Engineering and Chemical Technology, Imperial College, London, S.W.7. (1738)

CROSS INFECTION REFERENCE LABORATORY

We have a vacancy for a Technician or Senior Technician in the Streptococcus Laboratory. This post would be suitable for a candidate who is working for the I.M.L.T. Special Examination. Graduates may apply for this position. Salary according to qualifications and experience. National Health Service terms and conditions of service and superannuation.

Applications to Personnel Officer, Central Public Health Laboratory, Colindale Avenue, London NW9 5HT, stating age, qualifications and experience, and names and addresses of two referees. (1739)

CSIRO AUSTRALIA**DIVISION OF ENVIRONMENTAL MECHANICS
—BLACK MOUNTAIN, A.C.T.****RESEARCH SCIENTIST**

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas. The Organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD:**PLANT OPTICS****GENERAL:**

The Division conducts basic investigations of biological and physical processes in the soil-plant-atmosphere system. Energy, water, gas, and solute transfer and their interactions in the system form a major field of study. Laboratory facilities for soil physics, gas physics, solar radiation, fluid mechanics, micrometeorology and physiology are available. In addition, three mobile laboratories are available for field studies. The Division is linked to the Cyber 76 computer network and has access to CERES, CSIRO's largest controlled environment facility. The present staff of the Division is 24, mostly scientists and technicians.

DUTIES:

To undertake field and laboratory studies of light with reference to plant growth. Particular research topics will be the physics of the interception, transmission and diffusion of light in plant communities; the optical properties of individual leaves and their effects on spectral composition in the community and the development of suitable field and laboratory light-measuring equipment. The work will be linked closely to the Division's current research on the radiation balance of plant stands, water movement through plants, and the micrometeorology and physiology of CO₂ exchange by crops.

QUALIFICATIONS:

A Ph.D. degree or equivalent qualifications in appropriate fields, together with demonstrable research ability.

SALARY:

The appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist \$A9,380—\$A14,290 p.a. An outstanding applicant may be offered appointment at a higher level.

TENURE:

This is a three year appointment.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting reference number 416/14, should reach:—

**The Personnel Officer,
Australian Scientific Liaison Office,
64-78 Kingsway, LONDON, WC2B 6BD.
by the 28th December, 1973**

**Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.**

(1764)

**UNIVERSITY OF
NEWCASTLE UPON TYNE
DEPARTMENT OF MEDICINE
RESEARCH ASSOCIATE**

Applications are invited from graduates with an Honours degree in Biochemistry or Chemistry for a post as Junior Research Associate/Research Associate to assist in research into renal bone disease being undertaken in the Department of Medicine. The successful candidate will be based mainly in the Renal Laboratories of the Department and will be required to participate in the development of, and performance of, biochemical methods. The appointment, which will be for a period of up to five years, provides an opportunity to work for a higher degree in the case of those who do not already hold such a qualification. Salary will be according to qualifications and experience on the scale £1,380 to £1,629 per annum for a Junior Research Associate or £1,929 to £2,223 per annum for a Research Associate.

Applications should be submitted within three weeks of the appearance of this advertisement to Professor D. N. S. Kerr, Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, from whom further information may be obtained if required. (1793)

ROYAL POSTGRADUATE MEDICAL SCHOOL

TECHNICIAN required, with special interest in Biochemistry and tissue culture, to assist research Biochemist investigating Prostatic Tissue. Minimum qualifications O.N.C./H.N.C./A.I.M.L.T. or equivalent. Training given in advanced laboratory techniques. Salary according to age and qualifications. Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 3/326/N. (1804)

ROYAL POSTGRADUATE MEDICAL SCHOOL

SCIENTIFIC OFFICER (Ph.D. or B.Sc. chemist), required to join group studying drug metabolism in animals and man. Duties include the development of gas chromatographic assay methods for drugs and metabolites in biological fluids. Salary according to qualifications and experience, within scale £1,812 to £3,018. Applications to the School Secretary, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference number 20/279/N. (1757)

ZOOLOGIST /ORNITHOLOGIST

required by

MEDICAL RESEARCH COUNCIL IN KENYA

Applications are invited for the post of Zoologist/Ornithologist on the Medical Research Council Project, Kisumu, Kenya.

The Project has been established to study the short and long-term effects of large scale irrigation on the pattern of infectious diseases, particularly arbovirus infections and their mosquito and wild vertebrate hosts, on the Kano Plain near Kisumu. Studies of other diseases, infectious and non-infectious, are likely to be attracted to the Project as it develops. It is anticipated that the study, which started in 1971, will take not less than ten years to complete.

The post for a zoologist/ornithologist is to work with a team investigating the long-term ecological effects of irrigation of a previously largely arid region, particularly in relation to their effects on human health patterns. There are several important zoonoses in the area and ecological and microbiological studies of their hosts form an essential aspect of the work.

The zoologist/ornithologist will be expected to be able to design, organise and supervise experiments to measure population and behavioural changes in birds and small mammals likely to affect the risk of infection to man. He/she will also be expected to provide regular samples of blood and tissue specimens from wild and domestic animals and birds for microbiological investigations. It is also hoped that the successful candidate will acquire some expertise in the related fields (entomology, virology, demography, epidemiology, etc.) inherent in the study. Although a member of a team working to an overall agreed plan, he/she could expect to have areas of research which would be particularly his/her own.

The present staff of the Project consists of a Project Leader/Medical Officer, 2 Entomologists, 2 Technical Research Assistants (Chief Technicians) and a Project Manager and there is also attached a Medical Officer, 2 Voluntary Service Overseas Nurses and a Malacologist. The team is supported by over fifty locally-recruited subordinate staff. The Project is supported by laboratory work at the London School of Hygiene and Tropical Medicine and at the Microbiological Research Establishment, Porton.

The post is immediately available. Initial tour 30 months with paid home leave at end of tour. Free passages both ways. Starting salary according to age, qualifications and experience. Overseas and education allowances provided with free passages for children at U.K. boarding schools. F.S.S.U. Rent-free furnished accommodation. Further details of conditions of service will be given to candidates at interview.

For application form please write to Miss Elizabeth England, Medical Research Council, 20 Park Crescent, London W1N 4AL, quoting reference: E.743/44.

MRC

Medical Research Council

(1741)

Research Assistant

The Searle Group is a leading research-orientated company in the pharmaceutical industry, based in High Wycombe.

A department of our research laboratories investigating the growth of cells in tissue culture both in the laboratory and in a pilot plant requires help in adapting new cell lines to culture conditions. The applicant should have a BSc or HNC in Microbiology or Applied Biology. Ideally he should have experience in tissue culture techniques although this is not a prerequisite for the appointment.

Please apply to: Mrs E. M. Parr,
Personnel Manager, G. D. Searle & Co. Ltd.,
Lane End Road, High Wycombe, Bucks,
telephone High Wycombe 21124.

SEARLE

(1766)

MEDICAL RESEARCH COUNCIL

Laboratory Animals Centre

Applications are invited from science graduates (including agriculture) of not less than 28 years of age, for the post of Technical Officer in the Accreditation Department. The post will involve visiting laboratory animal breeding establishments and advising breeders on problems associated with laboratory animal production and supply.

Postgraduate experience with animals or in biological research would be an advantage but not essential.

Salary within the range £2,184 to £3,057 plus London Weighting and superannuation.

Applications, together with a copy of curriculum vitae and the names of two professional referees should be addressed to the Director, M.R.C. Laboratory Animals Centre, Medical Research Council Laboratories, Woodmansterne Road, Carshalton, Surrey SM5 4EF.

(1725)

UNIVERSITY OF MANCHESTER

There is a vacancy for a Technician in the Electron Microscope Unit of the Botany and Zoology Departments. Applicants should have at least O.N.C. or equivalent qualification and preferably H.N.C., and have had six years' relevant experience, including ultramicrotomy and other preparatory techniques.

Salary scale £1,848 to £2,163 per annum.

Applications, with full details of age, qualifications and previous experience, should be sent to Dr. R. Butler, Department of Botany, The University, Manchester M13 9PL, as soon as possible.

(1749)

MURDOCH UNIVERSITY PERTH, WESTERN AUSTRALIA

Applications are invited for two appointments, at the level of LECTURER or SENIOR LECTURER, as described below. Murdoch University will admit its first undergraduates in 1975. Further posts in these and other Schools will be advertised shortly.

SCHOOL OF MATHEMATICAL AND PHYSICAL SCIENCES

Foundation Professors: Chemistry, A. J. Parker; Mathematics, A. P. Robertson; Physics, B. Mainsbridge.

CHEMISTRY: Applicants should have interests in one or more of the following areas: analytical methods, inorganic mechanisms, mineral chemistry, solid state chemistry, electrochemistry, thermodynamics, kinetics or theoretical chemistry. (The School has a Mineral Chemistry Research Unit, supported by funds from Government and Industry.) The appointee will be expected to advise on the development of physical and/or inorganic chemistry, including the planning of new courses and the establishment of new laboratories, facilities and services.

MATHEMATICS: Applicants should have qualifications and research interests in mathematical statistics, or in some related branch of the applications of mathematics to the social and behavioural sciences. The person appointed will take part in planning mathematics and statistics courses at all levels.

GENERAL INFORMATION:

Salary ranges: Senior Lecturer \$A12,268 to \$A14,908 per annum; Lecturer \$A8,698 to \$A11,984 per annum.

Prospective applicants should write for further particulars and method of application to the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close on December 31, 1973. (1798)

CROSS INFECTION REFERENCE LABORATORY

We have a vacancy for a Technician in the Streptococcus Laboratory. Applicants with university degree, Institute of Medical Laboratory Technology qualifications or relevant experience an advantage. Salary according to qualifications and experience. National Health Service terms and conditions of service and superannuation.

Applications to Personnel Officer, Central Public Health Laboratory, Colindale Avenue, London NW9 5HT, stating age, qualifications and experience, and names and addresses of two referees. (1740)

SCOTTISH HORTICULTURAL
RESEARCH INSTITUTE
WEST OF SCOTLAND UNIT
AUCHINCROVE, AYR KA6 5AE

SCIENTIFIC
OFFICER

An S.O. is required to assist with the strawberry breeding programme. Duties include screening seedlings for disease resistance and recording fruit characteristics.

Qualifications: A pass degree, H.N.C. or equivalent is required. Field and/or glasshouse experience desirable.

Salary: £1,318 to £2,177 per annum. Superannuation scheme with an allowance to offset contribution.

Further particulars may be obtained from the Officer-in-Charge, with whom applications, naming two referees and stating age, education and experience, should be lodged by December 18, 1973. (1777)

THE BRITISH COUNCIL
SOIL MICROBIOLOGY
A LECTURER

is required at the UNIVERSITY OF CEYLON, PERADENIYA, SRI LANKA to lecture to students reading for a first degree. Candidates should be citizens of and normally resident in U.K., have a Ph.D. from a university in Britain and have relevant teaching experience.

SALARY: £2,714 to £4,710 per annum according to experience. Married overseas allowance £770-£97 according to family circumstances. The usual allowances and benefits will be granted including accommodation, travel and children's allowances. One or two-year contract. 73 OU 43.

Write, quoting relevant reference number to: The British Council (Appointments), 29 Bressenden Place, London SW1E 5DD, for further particulars and application form, to be completed as soon as possible. (1818)

MACQUARIE UNIVERSITY
SYDNEY, AUSTRALIA
CHAIR OF CHEMISTRY

Applications are invited for the above-mentioned appointment in the School of Chemistry.

The School of Chemistry is attempting to present an integrated view of Chemistry. The university is, therefore, seeking a candidate who has demonstrated ability to guide research and teaching over a fair range of the subject, and to forge interdisciplinary links with other areas of science.

The school is an active participant in the university's continuing developmental and investigational programmes designed to improve the quality of science teaching.

Further details of the responsibilities and framework within which the appointment is to be made are included in the additional information available to applicants.

The university reserves the right to fill any position by invitation.

The salary for the Chair will be \$A19,102 per annum.

Further information about the university and advice regarding the method of application should be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF, or from the Registrar, Macquarie University, North Ryde, N.S.W. 2113, Australia.

Applications close on January 18, 1974. (1733)

UNIVERSITY OF THE WEST INDIES
JAMAICA

Applications are invited for the post of PROFESSOR OF BIOCHEMISTRY in the Faculty of Medicine. Appointee will be expected to give leadership in the teaching and research activities of the Department of Biochemistry which prepares students for the M.B., B.S. degree and the B.Sc. General degree of the University. Salary scales (under review): Medically qualified, £5,000 to £6,250 per annum. Non-medically qualified, £4,250 to £5,750 per annum. Child allowance, F.S.S.U. Family passages; triennial study leave.

Detailed applications (6 copies), including a curriculum vitae and naming 3 referees, should be sent, by airmail, as soon as possible to the Registrar, University of the West Indies, Kingston 7, Jamaica, W.I. Detailed particulars of the post are available and should be obtained from the same source before

NEW ZEALAND

Department of Scientific and Industrial Research

Applications are invited for the undermentioned vacancies:

TWO SCIENTISTS

are required to work in Divisions located at Palmerston North

VACANCY 5416: PLANT PHYSIOLOGY DIVISION PLANT POPULATION GENETICIST

Salary: Up to \$11,671 p.a., depending on qualifications and experience.

Duties: This is a research position for a geneticist interested in producing and evaluating populations with differing physiological characteristics—particularly feed grain and forage crops.

Excellent research facilities, including major controlled environment areas, are available. Collaborative prospects are good—there being a staff of 50, half of whom are research scientists.

Qualifications desired: A Ph.D. with research experience is preferred.

VACANCY 5417: APPLIED BIOCHEMISTRY DIVISION NUTRITIONAL BIOCHEMIST

Salary: Up to \$10,953 p.a., depending on qualifications and experience.

Duties: The appointee will work in the field of protein nutrition—in the analysis of animal and human foodstuffs, and the development of alternative feed-protein and protein foods.

Qualifications desired: A Ph.D. in protein nutrition and/or protein chemistry, with experience in the use of experimental animals such as rats or chicks preferred.

Passages: Fares for both appointees and their wives and families will be paid.

Incidental expenses: Up to NZ\$120 for a single man and up to NZ\$800 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and general information are available from the High Commissioner for New Zealand, New Zealand House, Haymarket, London SW1Y 4TQ, with whom applications will close on January 11, 1974.

Please quote reference B13/18/129 when enquiring.

(1729)

STELLENAUSSCHREIBUNG

Am Institut für Biologie III (Genetik, Molekularbiologie, Biophysik) der Universität Freiburg i.Br., ist die Stelle eines

Wissenschaftlichen Rats und Professors (H2/H3)

zu besetzen.

In der Lehre soll sich der Stelleninhaber sowohl am Grundunterricht des Instituts (Abhaltung eines Kurses) wie auch an der Fortgeschrittenenausbildung (Grosspraktikum und spezielles Seminar) beteiligen.

Erwünscht wäre ein experimentelles oder theoretisches Forschungsgebiet mit Bezug auf höhere Systeme, das sich in den Rahmen des Sonderforschungsbereich "Molekulare Grundlagen der Entwicklung" einfügt.

Zum Beispiel:

Genetik und Entwicklung spezifisch menschlicher Eigenschaften.
Genetik und Entwicklung des Zentralnervensystems oder der Verhaltenssteuerung bei höheren Tieren oder Menschen.
Genetische und epigenetische Programmierung der Entwicklung von Zellen und Zellverbänden.
Genetik der Tumorentstehung.

Bewerbungen mit Publikationsliste, wissenschaftlichen Werdegang und Skizzierung zukünftiger Forschungspläne sind zu richten an das Dekanat der Universität Freiburg, 78 Freiburg i.Br., Schänzlestrasse 9-11.

Letzter Bewerbungstermin: 15.3.1974.

(1806)

CSIRO

AUSTRALIA

DIVISION OF BUILDING RESEARCH
—HIGHTT, VIC.**RESEARCH SCIENTIST**

The Commonwealth Scientific and Industrial Research Organization has a broad charter for research into primary and secondary industry areas. The Organization has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD:**URBAN SYSTEMS****GENERAL:**

The research programme of the Division, located at Hightt, Victoria, includes research on urban and regional planning using systems techniques. This work is directed towards a better understanding of the components and interactions involved in urban processes, and involves mathematical modelling of these processes as an aid to improved urban and transportation planning. The identification and measure of factors affecting quality of life is also included in these studies. Continued collaboration with planners in the application of the techniques developed to new and existing cities is expected.

DUTIES:

To develop and apply systems techniques to new urban and regional planning projects, with particular emphasis on the use of computer-implemented mathematical models. The opportunity is available to participate in the development of new and rational aids to decision making in a creative environment, and for applying them to a range of pressing urban problems.

QUALIFICATIONS:

A Ph.D. degree or equivalent research experience in engineering, planning or science, together with demonstrable research ability. Applicants should have ability in mathematics and computer programming together with appropriate experience.

SALARY:

The appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A9,380–\$A14,290 p.a.

TENURE:

This position is available for an indefinite period and Australian Government Superannuation benefits are available.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting reference number 390/711, should reach:—

The Personnel Officer,
Australian Scientific Liaison Office,
64-78 Kingsway, LONDON WC2B 6BD
by the 28th December, 1973

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(1765)

UNIVERSITY OF NAIROBI
KENYA

Applications are invited for SENIOR LECTURESHIP IN PIG PRODUCTION IN DEPARTMENT OF ANIMAL PRODUCTION. Applicants, who must either be Veterinary or Agriculture graduates, should possess a Ph.D. in any field of Pig Production. Candidates holding lower qualifications (not less than an M.Sc.) will only be considered if they have several years of research experience and teaching at university level in Pig Production. Salary scale: K£2,256 to K£3,036 per annum (K£1=£1.18 sterling). The British Government may supplement salary by £950 per annum (sterling) for married appointee or £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. F.S.S.U. Family passages; various allowances.

Detailed applications (2 copies) including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than December 31, 1973, to the Registrar, University of Nairobi, P.O. Box 30197, Nairobi, Kenya. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of the appointment may be obtained from either address.

(1787)

UNIVERSITY OF SYDNEY
AUSTRALIA**LECTURESHIP IN THE FIELD OF
VETERINARY PATHOLOGY AND
MICROBIOLOGY**

Appointee to be responsible for both lecture and practical courses under the direction of the Head of the Department of Veterinary Pathology. Basic veterinary qualifications or equivalent required. Preference given to applicants with sound knowledge and experience in the fields of viral diseases or general immunology.

The position advertised is permanent but in appropriate cases an initial three-year appointment may be made with possibility thereafter of permanency, or in certain cases return fares.

Salary range: \$A8,698 to \$A11,982 per annum. Applications, including curriculum vitae, list of publications and names of three referees, by December 20, 1973, to the Registrar, University of Sydney, N.S.W. 2006, Australia, from whom further information available. Information also available from Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

(1782)

UNIVERSITY OF DUNDEE
DEPARTMENT OF MEDICINE**RESEARCH
ASSISTANT**
(Biochemistry)

Honours graduates in Biochemistry are invited to apply for a three-year appointment to the above post. The person appointed will work in the research laboratories of the Department of Medicine (Professor I. A. D. Bouchier) on a study of bile salt metabolism, involving the estimation and separation of bile salts and the measurement of bile salt pool sizes. Relevant experience would be advantageous.

The post is financed by the M.R.C. and carries a starting salary of up to £1,572 per annum. Applications, quoting Ref. Est./74/731, and containing the names and addresses of two referees, as well as details of qualifications and experience, should be sent to the Secretary, The University, Dundee DD1 4HN, by December 21, 1973.

(1736)

UNIVERSITY OF HONG KONG

Applications are invited for the following new posts:

TWO LECTURESHIPS/ASSISTANT LECTURESHIPS IN ELECTRICAL ENGINEERING. Candidates should have a higher degree and/or corporate membership of the Institute of Electrical Engineers, with experience in digital electronics and/or data processing and transmission. Preference will be given to those who have industrial experience or research interest in direct digital control of power systems or other industrial processes. Successful candidates may be required to teach both undergraduate and postgraduate courses, as well as supervise higher degree students.

THREE LECTURESHIPS/ASSISTANT LECTURESHIPS IN INDUSTRIAL ENGINEERING. Candidates must have an appropriate first degree and the further qualification or experience specified for the individual posts, which are:

LECTURESHIP/ASSISTANT LECTURESHIP IN WORK DESIGN AND ERGONOMICS. At least three years' industrial or research experience in the field; or a higher degree and some experience of applications.

LECTURESHIP/ASSISTANT LECTURESHIP IN QUALITY AND RELIABILITY ENGINEERING. At least three years' experience in quality assurance and/or reliability engineering, or a higher degree and some record of research and/or application in this field.

LECTURESHIP/ASSISTANT LECTURESHIP IN INDUSTRIAL COST ANALYSIS. Associate membership of a professional accounting institution or corporate membership by examination of the Institute of Cost and Management Accountants or equivalent; experience in an industrial company or consultancy is desirable.

Annual salaries (superannuable) are: Lecturer: HK\$40,800 by HK\$2,760 to HK\$46,320 bar HK\$49,080 by HK\$2,760 to HK\$68,400; Assistant Lecturer: HK\$29,760 by HK\$2,760 to HK\$38,040. At the time of issue the rate of exchange is £1=HK\$12.15 approximately.

Starting salary will depend on qualifications and experience. Salaries for female appointees below HK\$62,880 are slightly lower than given above; equalisation of male and female salary scales will be achieved by April 1, 1975.

Further particulars and application forms may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF, or the Secretary to the Council, University of Hong Kong.

Closing date for applications is 31 December 1973.

(1732)

UNIVERSITY OF QUEENSLAND
AUSTRALIA**READER/SENIOR LECTURER
IN MATHEMATICAL STATISTICS
DEPARTMENT OF MATHEMATICS**

Applicants should have good research records and be experienced in the field of stochastic processes.

Salary: Reader—\$A15,940 per annum; Senior Lecturer—\$A12,268 to \$A14,308 per annum.

Other Benefits: Superannuation similar to F.S.S.U., housing assistance, study leave, and travelling and removal expenses.

Additional information and application forms are obtainable from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in London and in Brisbane on February 1, 1974.

(1813)



RESEARCH ASSOCIATE (Post Doctoral)

to join a group studying properties of semiconductor injection lasers and to be responsible for observations on the spectral mode structure of the laser output. The appointment is for one year. Previous experience useful but not essential.

**Salary: Within range
£1,929 to £2,058 to £2,223**

Requests (quoting Ref. N) for details and application form (returnable by December 18, 1973) to Personnel Section, U.W.I.S.T., Cardiff CF1 3NU. (1755)

UNIVERSITY OF THE WEST INDIES JAMAICA

Applications are invited for the following posts:

1. PROFESSOR OF PHYSICS. The Department prepares students for the B.Sc. General and B.Sc. Special Degrees of the University and has students enrolled in M.Sc. and Ph.D. programmes. The present departmental research interests include Atmospheric Physics, Radio Astronomy and Biophysics and future expansion into an Applied Physics area is planned. The appointee will be expected to give academic leadership in the development of applied physics within the Department, at both an undergraduate and graduate level. The preferred field of specialisation is Materials Science but an appointment in another branch of applied physics is not precluded.

2. LECTURER/ASSISTANT LECTURER IN THE DEPARTMENT OF CHEMISTRY. Applicants with interest in Physical Chemistry would be preferred.

Salary scales (under review): Professor, £4,250 to £5,750 per annum. Lecturer, £1,850 to £3,265 per annum. Assistant Lecturer, £1,500 to £1,660 per annum. Child allowance. F.S.S.U. Family passages; triennial study leave.

Detailed applications (6 copies), including a curriculum vitae and naming 3 referees, should be sent, by airmail, as soon as possible to the Registrar, University of the West Indies, Mona, Kingston 7, Jamaica, W.I. Detailed particulars of the posts are available and should be obtained from the same source before an application is made. (1780)

MEMORIAL UNIVERSITY OF NEWFOUNDLAND CANADA

DEPARTMENT OF PHYSICS GEOPHYSICIST

Applications are invited for a faculty appointment in solid-Earth geophysics, effective September 1, 1974, rank and salary to be negotiable and commensurate with the qualifications of the appointee. A Ph.D. in geophysics, with a strong physics background, or in physics with geophysical research experience (preferably but not necessarily in an academic setting), is required. Preference will be given to applicants interested in collaborating in a field programme using primarily seismological methods for investigating crustal structure in coastal areas. The Department's present research capabilities are in rock- and palaeomagnetism, magnetotellurics, gravity, theoretical global Earth and planetary physics. The appointment will include teaching duties at the graduate and undergraduate level in an expanding programme. The Department offers programmes leading to the M.Sc. and Ph.D. degrees.

Applications, including curriculum vitae and the names of three referees, should be addressed to Professor S. W. Breckon, Head, Department of Physics, Memorial University of Newfoundland, St. John's Newfoundland, Canada. (1783)

UNIVERSITY OF NEWCASTLE UPON TYNE DEPARTMENT OF CHEMICAL ENGINEERING

Applications are invited from graduates for appointment to a Research Associateship in the Department of Chemical Engineering. The person appointed should have a good knowledge of the principles of physics and will work with Professor J. D. Thornton on the applications of laser techniques to the study of droplet surfaces and droplet dynamics in two-phase liquid-liquid systems. The research project is sponsored by the Science Research Council and the appointment will be for three years in the first instance.

The post is open to persons of either sex and carries F.S.S.U. benefits. The starting salary will be within the scale £1,929 to £2,223.

Applications and requests for further information should be addressed to Professor J. D. Thornton,

NEW ZEALAND

Ministry of Agriculture and Fisheries

Applications are invited for the undermentioned vacancy:

DIRECTOR WALLACEVILLE ANIMAL RESEARCH CENTRE

The position of Director, Wallaceville Animal Research Centre will become vacant in January 1974 following the retirement of Dr M. B. Buddle, D.Sc., B.V.Sc., F.A.C.V.S.

The Wallaceville Animal Research Centre, located in the Hutt Valley, 20 miles from Wellington is the main centre in New Zealand concerned with both basic and applied research on animal diseases and animal products and environmental contamination.

The major research sections headed by senior scientists include experimental biology (infectious diseases, immunology, experimental pathology and metabolic syndromes), experimental epidemiology, parasitology, nutritional biochemistry, insecticides and toxicology, apiculture and the hydatid research unit.

The Research Centre has a professional staff of 50 scientists, 60 technicians and a total staff of 200. The Central Brucellosis Laboratory and the Reference Laboratory of the Animal Health Division are also located on the Wallaceville campus.

New facilities recently completed at Wallaceville include Stage I of the laboratory, administration and library block, insecticide laboratory. Additional buildings are in the course of construction with an expected expenditure over the next four financial years in excess of \$2,000,000. Land available for research currently exceeds 245 hectares.

Salary: The position will command a salary of up to NZ\$15,025.

Duties: The appointee will be responsible to the Director of the Research Division of the Ministry for the research activities of the Wallaceville Centre and will act in a consultative capacity to the Ministry on matters affecting animal health.

Qualifications desired: The appointee should possess a basic Veterinary qualification together with appropriate post-graduate qualifications and have a record of personal research achievement and leadership.

Passages: Fares for appointee and his wife and family will be paid.

Incidental expenses: Up to NZ\$120 for a single man and up to NZ\$800 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and general information are available from the High Commissioner for New Zealand, New Zealand House, Haymarket, London SW1Y 4TQ, with whom applications will close on January 11, 1974.

Please quote reference B13/2/205/5434 when enquiring.

(1730)

THE WELSH NATIONAL SCHOOL OF MEDICINE (University of Wales)

DEPARTMENT OF PATHOLOGY

Applications are invited for a

RESEARCH ASSISTANT

in connection with an MRC project, for a period of two years. Salary £1,278 to £1,980 (under review) The appointment entails research on lymphocyte function for a variety of diseases notably sarcoidosis. Excellent facilities available in this new teaching centre.

Application forms available from the Registrar, The Welsh National School of Medicine, Heath Park, Cardiff, CF4 4XN, and should be returned within two weeks of the appearance of this advertisement. (1745)



Wellcome

Department of Bacteriology

A vacancy has arisen in the Department of Bacteriology for a Research Graduate with a veterinary or scientific qualification to undertake research and to support both the production and field investigation of bacterial vaccines. The Company's products cover a wide range of interests including Fusiformis, Clostridia, E. coli and Salmonella prophylactics. The person appointed will work initially in the anaerobic section of the Department, where he will be concerned with the Company's 'Clovax' Foot-rot Vaccine.

The position carries a high degree of responsibility and an appropriate salary will be offered, together with other attractive conditions of employment.

Applications, giving brief details of background and experience, should be sent to:

**The Personnel Manager,
THE WELLCOME RESEARCH LABORATORIES,
Langley Court,
Beckenham,
Kent BR3 3BS.**

(1821)



**ST. MARY'S HOSPITAL
PADDINGTON, W.2**

BASIC GRADE PHYSICIST

A Physicist is required in the Department of Clinical Physics which is mainly concerned with the diagnostic uses of radioisotopes but has a steady commitment in radiotherapy treatment planning. There is a large commitment to scanning procedures for which a gamma camera and a linear scanner are available, but there are some research and development activities.

Data processing methods for renograms are available.

Salary scale: £1,278 per annum (minimum of probationary scale) to £2,370 per annum (maximum of post-prob. scale) depending on qualifications and experience, plus £126 per annum London Weighting Allowance. Salaries under review.

Applications stating age, qualifications and experience, and the names of two referees, to Group Establishment Officer by December 6, 1973.

(1759)

PHYSICIST OR ELECTRICAL ENGINEER

required for the development and application of electro-physiological measurement techniques in the diagnosis of central disorders of hearing. Good knowledge of electronics and computer technology essential. Salary in accordance with age and qualifications. F.S.S.U. superannuation. Applications to the Director, M.R.C. Hearing and Balance Unit, Institute of Neurology, National Hospital, Queen Square, London WC1N 3BG. (1737)

FOURAH BAY COLLEGE UNIVERSITY OF SIERRA LEONE

Applications are invited for a LECTURESHIP IN GEOLOGY tenable as soon as possible. Applicants should have a good honours degree in Geology or a good joint honours degree in Geology and Physics, and preferably a Ph.D. with postgraduate experience in Geophysics or Structural Geology. Candidates with an interest in Sedimentology may be considered. Salary scale (under review): Le2,400 to Le4,740 per annum (£1 sterling=Le2). The British Government may supplement salary in range £950 to £1,300 per annum (sterling) for married appointee or £350 to £700 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. F.S.S.U. Family passages; various allowances; regular overseas leave.

Detailed applications (2 copies) including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than December 31, 1973, to the Secretary, University of Sierra Leone, Private Mail Bag, Freetown, Sierra Leone. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of this appointment may be obtained from either address. (1785)

THE UNIVERSITY OF LEEDS DEPARTMENT OF MEDICINE (LEEDS GENERAL INFIRMARY) DIVISION OF DERMATOLOGY

Applications are invited for the post of RESEARCH ASSISTANT in Mycology. The successful candidate will take part in studies on the epidemiology and pathogenesis of Candida infections.

Applicants should have a degree in Microbiology or a related subject. The appointment will be made for one year in the first instance. Starting salary £1,449 (with F.S.S.U. benefits).

Forms of application and further particulars from the Registrar, The University, Leeds LS2 9JT (please quote 50/5/D). Closing date December 14, 1973. (1772)

Assistant in Regulatory Affairs Department

Smith Kline & French Laboratories Limited is a major international pharmaceutical company based in Welwyn Garden City. We now require an additional graduate to join our Regulatory Affairs Department, which is the principal interface between the company and the medicines licensing authorities.

The basic requirements are:

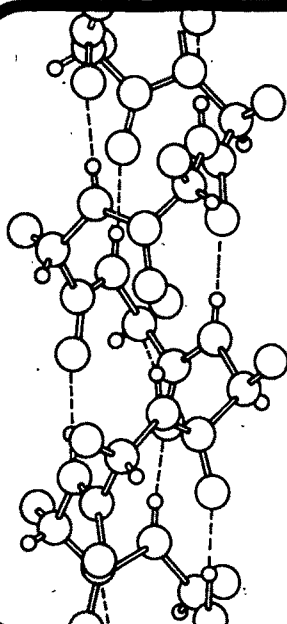
- a good honours degree in a biological science or pharmacy with, possibly, postgraduate experience in pharmacology
- the ability to present information in coherent, precise reports.

The work will entail the evaluation and editing of data from within the Company's own research and from other sources. Experience in the preparation of data for licensing bodies or experience with the requirements of the drug regulatory authorities would be a distinct advantage.

Salaries are competitive and will reflect ability and experience. Conditions of employment are in line with those expected of a large international organisation. Assistance with relocation expenses given where appropriate.

(1823)

Apply to the Personnel Officer,
Smith, Kline & French Laboratories Limited,
Mundells, Welwyn Garden City, Herts. Telephone: Welwyn Garden 25111.



Research vacancies for graduates

The food industry is expanding and our Research Laboratory of 1,350 people is actively participating in this expansion. Our Research Assistant vacancies are suitable for First Degree Graduates with or without additional experience.

Two Physical Chemists in our Dairy Technology Section

To focus on Molecular interaction and on product behaviour.

One job is to help unravel how polysaccharides interact with milk proteins and to correlate this with utilisation of these natural polymers in Dairy Products. Ref CWA 170.

The Second job is to relate the composition of the aqueous phase of protein systems to their subsequent behaviour in Dairy Products. Ref CWA 163.

A Physicist/Physical Chemist in our Oils and Fats Technology Section

To study the factors controlling the texture and structure of fat-based

foodstuffs such as creams, margarines etc. The job will involve the development and application of a variety of test techniques. Experience in rheology is preferred, but not essential. Ref CWA 173.

A Chemist/Biochemist in our Natural Products Section

To join a group providing technical support for a large multi-disciplinary project team involved in the development of non-food products from novel polysaccharide materials. Experience and competence in practical work are important qualities for this vacancy. Ref CWA 174.

An Organic/Physical Chemist in our Lipid Chemistry Section

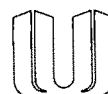
For studies on the chemistry and function of lipids, especially emulsifiers in convenience foods. A good background and experimental skill is essential. Experience both in organic and physical chemistry would be ideal for the job. Ref CWA 182.

Location

All vacancies (except CWA 173 and 182) are at Colworth House, Sharnbrook, which is ten miles north of Bedford. CWA 173 and 182 are based at Welwyn, Hertfordshire, which is twenty miles north of London.

Applicants

Should write for an application form and further details stating appropriate reference number to: The Personnel Officer, Unilever Research, Colworth/Welwyn Laboratory, The Frythe, Welwyn, Herts.



Unilever Research
Colworth/Welwyn Laboratory

MASSEY UNIVERSITY PALMERSTON NORTH, NEW ZEALAND SENIOR LECTURER/LECTURER IN ENTOMOLOGY

Applications are invited for the position of Senior Lecturer or Lecturer in Entomology in the Sub-Department of Plant Pathology. Applicants should have a postgraduate degree in Agricultural Science or Science, together with training and experience in applied entomological research particularly relating to plant production.

The appointee will be required to organise courses and teach in the general field of entomology to undergraduate and graduate students in the Faculty of Agricultural and Horticultural Science. The successful applicant will also be expected to develop an active research programme in the field.

An appointment may be made within the following salary ranges, depending on qualifications and experience: Senior Lecturer NZ\$8,249 to NZ\$9,723; Lecturer NZ\$6,335 to NZ\$8,103.

Further details of the position and the University together with general conditions of appointment, may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF, or from the Registrar of the University.

Applications close on **December 22, 1973.** (1795)

FLINDERS UNIVERSITY OF SOUTH AUSTRALIA

SCHOOL OF BIOLOGICAL SCIENCES

Applications are invited for the following position: **LECTURER IN BIOLOGY** (Bacteriology/Immunology). As part of its expanding interest in microbiology, the School invites applications from suitably qualified persons who could assist in the development of new courses for science and medical students in the general areas of bacteriology and immunology. Preference may be given to applicants with research interests in microbial immunology.

Salary scale: \$A8,698 to \$A11,982. Superannuation is on the F.S.S.U. basis.

Further information about this position, including conditions of appointment and details required of applicants may be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications should be lodged in duplicate with the Registrar, The Flinders University of South Australia, Bedford Park, South Australia, 5042, not later than **December 21, 1973.** (1796)

UNIVERSITY OF EAST ANGLIA

Applications are invited for a

CHAIR IN BIOLOGY

tenable in the School of Biological Sciences from October 1, 1975 or such other date as may be arranged. It is proposed to appoint a person with interests in one or more of the fields of biophysics, animal physiology and cell biology.

Details from the Registrar and Secretary, University of East Anglia, Norwich NR8 8C, with whom applications (one copy only) together with the names and addresses of three persons to whom reference may be made, should be lodged not later than **December 31, 1973.** (1752)

Glaxo

Immuno-Pharmacology

A graduate pharmacologist or immunologist is required for a senior position concerned with the development of drugs of potential therapeutic value in the treatment of allergic and auto-immune diseases. The successful applicant will be expected to initiate new lines of approach and previous experience in this or a related field is considered essential.

The starting salary will be related to qualifications and experience, and will be fully commensurate with the senior nature of the post. Excellent working conditions in new and well-equipped laboratory and animal facilities will also be provided.

The Company offers other benefits which include contributory pension scheme, profit sharing bonus scheme, catering and sports club facilities.



Please write, giving brief details, quoting ref. U.385, to:

The Senior Personnel Officer (Research),
GLAXO LABORATORIES LIMITED,
Greenford, Middx., UB6 OHE.

(1775)

Im Fachbereich Biologie der Philipps-Universität Marburg/Lahn
ist zum Wintersemester 1974 eine

H 4—Professur (Hess.Bes.G.) für Mikrobiologie

zu besetzen.

Der Bewerber sollte aufgrund mehrjähriger Fach Erfahrung in der Lage sein, die Mikrobiologie in Lehre und Forschung angemessen zu vertreten.

Dazu gehören:

Eingliederung des Fachs in die Studienordnung des Fachbereichs,
Detailplanung und Ausstattung eines im Rohbau vorhandenen Neubautraktes.
Aufbau und Leitung eines Forschungsteams.

Die üblichen Bewerbungsunterlagen sind bis zum 15. Februar 1974 an den Herrn Präsidenten der Philipps-Universität, 355 Marburg/Lahn, Biegenstr. 10, zu richten. (1826)

Scientific Writing

up to £2600 plus bonus

A key appointment has arisen in our Research and Development Services Division, resulting from the planned expansion of the company's research activities.

The task is to compile and edit scientific reports for submission to UK and overseas regulatory authorities. It involves working closely with the scientists of the various disciplines engaged in pharmaceutical research, as well as some contact with outside authorities. The ability to write clear and concise English and an eye for detail are essential.

Applicants should be graduates in one of the biological sciences with a minimum of 2 to 3 years' experience in a research environment. Particular experience in Product Registration work would be desirable but not essential.

The Research and Development Services Division is pleasantly situated in new laboratories at Ware, Hertfordshire. An excellent commencing salary will be offered together with the fringe benefits one would expect from a major pharmaceutical company, including a share in the profitability of the Glaxo Group of which we are a member, and relocation assistance where appropriate.



Please write briefly, quoting reference U.384, to:

G. R. Jones, Personnel Officer,
Allen & Hanburys Research Ltd.,
Ware, Herts. SG12 0BJ.



(1820)

Coláiste na hOllscoile Gaillimh
(University College Galway)

TRAINEE TECHNICIAN

Applications are invited for the post of Trainee Technician in the Department of Physics.

Candidates should be at least 18 years old and have passed the Leaving Certificate, Matriculation examination or G.C.E. (with two science subjects).

Salary: £984 by £72 to £1,272.

Applications should be sent, as soon as possible, to Professor of Electron Physics, University College, Galway.

(1809)

THE MEDICAL RESEARCH COUNCIL requires a Technician and two Junior Technicians for biochemical research on inherited variations in human enzymes.

Apply in writing, giving qualifications, age and experience, to:

Professor Harry Harris,
M.R.C. Human Biochemical Genetics Research Unit,
Wolfson House, 4 Stephenson Way, London NW1 2HE.

(1790)

UNIVERSITY OF SYDNEY
AUSTRALIA

DEPARTMENT OF AGRONOMY AND
HORTICULTURAL SCIENCE

LECTURESHIP IN HORTICULTURE
(Plant Physiologist)

Applicants for the above-mentioned post should have training in Plant Physiology or Plant Biochemistry, and an interest in undertaking basic research on problems of practical significance in horticultural crop production or environmental horticulture. Experience in the fields of photosynthesis or plant hormones an advantage, but applicants with other interests considered.

The position advertised is permanent, but in appropriate cases an initial three-year appointment may be made with possibility thereafter of permanency or in certain cases return fares.

Salary range: \$A8,698 to \$A11,982 per annum.

Applications, including curriculum vitae, list of publications and the names of three referees, by December 31, 1973, to the Registrar, University of Sydney, N.S.W. 2006, Australia, from whom further information available. Information also available from the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

(1781)

THE POLYTECHNIC OF
NORTH LONDON

Holloway, London N7 8DB

Department of Biology and Geology

Temporary Lecturer in Biology

required for the summer term 1974, a temporary Lecturer Grade II with special interests in animal and quantitative ecology. Duties will include teaching environmental biology at degree level and assisting on field courses. The appointment will date from April 1 to August 31, 1974.

Application forms and further details can be obtained from the Establishment Officer, The Polytechnic of North London, Holloway Road, N7 8DB.

(1763)

THAMES POLYTECHNIC

Research Assistant in Chemistry

Applications are invited from holders of good honours degrees and graduates of the R.I.C. for two posts of Research Assistant in the fields of:

- The inhibition of the corrosion of iron.
- The kinetics of the action of fuel additives.

Successful candidates will work towards a higher degree of the C.N.A.A. and contribute six hours each week to the teaching programme of the School of Chemistry.

Salary: £1,427 by £55 (2) to £1,537 per annum.

Further particulars and form of application may be obtained from the Secretary, Thames Polytechnic, Wellington Street, London SE18 6PF to whom completed applications should be returned as soon as possible. (1789)



LOUGHBOROUGH
UNIVERSITY OF
TECHNOLOGY

LECTURER IN PHYSICS

Applications are invited for the post of LECTURER in the Department of Physics. Duties will include lecturing to undergraduate courses in physics and engineering physics and to develop collaborative research between the environmental physics department at Nottingham University School of Agriculture and this University.

It is expected that the successful applicant will have a special interest in optics and instrumentation. Salary within scale £1,929-£4,548.

Postcard requests for further particulars and application form to Assistant Registrar (Establishment), ref. 73/60.

Loughborough

Leicestershire
(1774)

UNIVERSITY OF ALBERTA
FACULTY OF DENTISTRY

DEPARTMENT OF ORAL BIOLOGY

Opportunities for research in:

BIOCHEMISTRY
MICROBIOLOGY
PHYSIOLOGY

for those who wish to receive training in health sciences research specialising in connective tissue biochemistry, neuromuscular physiology or nucleic acid chemistry leading to M.Sc. or Ph.D. degrees. Graduate assistantship support is available.

Address enquiries to Chairman, Department of Oral Biology, University of Alberta, Edmonton, Alberta, Canada T6G 2H7. (1792)

UNIVERSITY COLLEGE HOSPITAL
MEDICAL SCHOOL
SENIOR LECTURER

Applications are invited for the post of Senior Lecturer in the Department of Biochemical Pathology. The post includes teaching duties in General Pathology and responsibility in running a tissue culture unit dealing with a clinical biopsy unit. Preference will be given to candidates with experience in Cytochemistry and Radio-autography. Salary in the range £4,368 to £5,496 plus £162 London Weighting and the post is F.S.S.U. superannuated.

Applications in duplicate, including names of two referees, should be sent by December 21, 1973, to the Secretary, University College Hospital Medical School, University Street, London WC1E 6JJ. (1771)

Technicians

grade 2B, required by Paddington Technical College for general and specialised duties and training within the PHYSICS AND MATHEMATICS Department, which is a major centre for the training of laboratory technicians and for photography.

Salary scale £1,416 to £1,671, plus £174 London Weighting.

Application forms and further details from the Secretary to the Department (Ref. P/JRS), Paddington Green, London W2 1NB. (1773)

North East London Polytechnic

Department of Applied Biology

Research Assistant

Applications are invited from good honours graduates of Applied Biology, Pharmacy, Pharmacology or Medicine. The proposed research programme involves a study of the mode of action of non-steroidal anti-inflammatory agents using rats. The work includes an investigation into the relationship between prostaglandins and putative mediators of inflammation. It will be directed by Dr G. B. West. The successful candidate will be expected to register for a higher degree (CNA).

Commencing salary: £1,427 per annum.

Further details and application forms from: The Academic Staffing Officer, Ref: S/CF 125, North-East London Polytechnic, Forest Road, London E17 4JB. For return by 14 December, 1973. (1807)

UNIVERSITY OF NAIROBI KENYA

Applications are invited for SENIOR LECTURESHIP IN DEPARTMENT OF MATHEMATICS. Applicants should possess a postgraduate qualification in Pure Mathematics, Applied Mathematics or Statistics. They should also have considerable university teaching and research experience. Salary scale: K£2,256 to K£3,036 per annum (K£1=£1.18 sterling). The British Government may supplement salary by £950 per annum (sterling) for married appointee or £650 per annum (sterling) for single appointee (normally free of all tax) and provide children's education allowances and holiday visit passages. F.S.S.U. Family passages; various allowances.

Detailed applications (2 copies) including a curriculum vitae and naming 3 referees, should be sent by air mail, not later than December 31, 1973, to the Registrar, University of Nairobi, P.O. Box 30197, Nairobi, Kenya. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars of the appointment may be obtained from either address. (1786)

UNIVERSITY OF LEICESTER SCHOOL OF BIOLOGICAL SCIENCES BOTANY DEPARTMENT

Applications are invited for a SENIOR LECTURESHIP OR READERSHIP (within the scale £4,368 to £5,496 per annum) in Plant Taxonomy to take up appointment from October 1, 1974, or as soon thereafter as possible. The person appointed will be responsible for the teaching of taxonomy in the School and for the supervision of the Herbarium (approaching 10,000 specimens), and will be expected to help in the development of the University Botanic Garden.

Applications should reach the Registrar, University of Leicester, by February 23, 1974, from whom further particulars may be obtained. (1776)

CHAIRMAN—DEPARTMENT OF ANATOMY

Columbia University, College of Physicians and Surgeons, an equal opportunity employer, is seeking an individual as Chairman of Anatomy Department. Should be qualified medical scientist and experienced medical educator.

Send curriculum vitae to: Myron Winick, M.D., Chairman, Search Committee, Institute of Human Nutrition, 511 West 166th Street, New York, New York 10032. (1289)

British Museum (Natural History)

Educational Technologist

To join a team of scientists and designers engaged in the development and production of a comprehensive new exhibition scheme for natural history including biology and geology.

The successful candidate will assist in devising methods of presenting complex information using a range of audio-visual media, and monitor the proposed exhibits and related publications during preparation to ensure that they may be readily understood by the general public.

The successful candidate will probably be appointed as Senior Scientific Officer, be aged 26–31, hold a good honours degree in a scientific subject and, certainly, have at least four years postgraduate experience. Candidates with a scientific qualification of at least HNC level together with five years' relevant post-qualification experience, will, however, be considered for appointment as Higher Scientific Officer. Preference will be given to those with a broad knowledge of the biological sciences and experience as an educational technologist.

SALARY: SSO, £2,790–£3,815; HSO £2,251–£2,842.

For further details and an application form (to be returned by 21 December, 1973) write to Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, or telephone Basingstoke 29222, extension 500, or London 01-839 1992 (24-hour answering service). Please quote: SB/13/DK.

(1816)

UNIVERSITY OF NATAL

DEPARTMENT OF BIOLOGICAL SCIENCES DURBAN, SOUTH AFRICA

Applications are invited from suitably qualified persons for appointment to the post of

PROFESSOR OF BIOLOGY

Applicants should have an interest in the development of integrated courses in biology. Preference will be given to applicants interested in whole-organism biology and/or ecology.

The salary scale attached to the post is:

R8,100×300—R9,900 per annum

(Approximate rate of exchange: R1.61=£1.)

plus a 15% pensionable allowance on basic salary.

The commencing salary notch will be dependent on the qualifications and/or experience of the successful applicant. In addition, an annual vacation savings bonus up to R260 for married men and R130 for women and single men is payable, subject to Treasury regulations.

Application forms, further particulars of the post and information on pension, medical aid, staff bursary, housing loan and subsidy schemes, long leave conditions and travelling expenses on first appointment are obtainable from the Registrar, University of Natal, King George V Avenue, Durban, South Africa, with whom applications, on the prescribed form, must be lodged not later than January 31, 1974, quoting Ref. Adv. 115/73. (1758)

MEDICAL RESEARCH COUNCIL RADIOBIOLOGY UNIT, HARWELL

There is a vacancy for a Scientist in a small Group working on aspects of induction of chromosomal aberrations by ionizing radiations in a variety of cells. Some knowledge of conventional cytological techniques, including tissue culture, is very desirable, and a real interest in chromosome morphology is essential. Salary according to age and qualifications (Grade II £1,830–£3,378). Usual Medical Research Council Conditions of Service.

Applications, in writing, giving full details and names of two referees, should be addressed to: Administrator, Medical Research Council Radiobiology Unit, Harwell, Didcot, Berkshire, quoting Reference FDB/36, by December 31. (1791)

LUTON AND DUNSTABLE HOSPITAL

Biochemist Basic Grade

Salary according to qualifications, required in the Chemical Pathology Department from January 1, 1974. This post offers excellent experience in a wide range of automated and special biochemical procedures.

The successful candidate will be encouraged to attend the M.C.B. Course at St. Bartholomew's Hospital. Previous experience is not essential.

Written applications, stating age, qualifications and experience, together with two referees to the Hospital Secretary, Luton and Dunstable Hospital, Lewsey Road, Luton LU4 0DZ or telephone Luton 53211 Ext. 5 for further details.

An informal visit to the department is welcomed by arrangement.

(1748)

Department of Agriculture and Fisheries for Scotland
Freshwater Fisheries Laboratory, Pitlochry

Behavioural Physiologist

■ Join team working on juvenile salmonids growth and survival problems ■ Develop work on activity rhythms and feeding behaviour of smolts ■ Experiment at Almondbank Smolt Rearing Station on factors affecting growth and survival of Atlantic Salmon.

☐ 1st/2nd hon's degree or equivalent in Zoology ☐ At least 2 years' post-graduate experience ☐ Age under 30 ☐ Appointment as Higher Scientific Officer (£2076-£2667) ☐ Ref: SA/2/DLB ☐ Closing date 21 December 1973.

☐ Application forms from Scottish Office, Personnel Division, Room 172, St Andrew's House, Edinburgh EH1 3BX, telephone 031-556 8501 ext 2621.

Ministry of Agriculture, Fisheries and Food
Pest Infestation Control Laboratory, Slough

Statistician/Scientist

■ Head group collecting data on use of pesticides in food storage and public health ■ Plan and design surveys ■ Process and report on results ■ Supervise support staff.

☐ 1st/2nd hon's degree in Mathematics or Science ☐ At least 4 years' relevant postgraduate experience ☐ Knowledge of data processing, scientific information work or use of statistics desirable ☐ Age 26 to 31 ☐ Appointment as Senior Scientific Officer (£2615-£3640) ☐ Ref: SB/4/AF ☐ Closing date 21 December 1973.

☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Department of Trade and Industry
Warren Spring Laboratory, Stevenage.

Analytical Chemist

■ Carry out gas chromatographic analysis for environmental research ■ Develop new techniques.

☐ 1st/2nd hon's degree in Chemistry ☐ Experience in gas chromatography ☐ Aptitude for practical laboratory work ☐ Age under 30 ☐ Appointment as Higher Scientific Officer (£2076-£2667) or Scientific Officer (£1318-£2177) ☐ Ref: SA/14/MF ☐ Closing date 21 December 1973.

☐ Application forms from The Director, Warren Spring Laboratory, Elder Way, Stevenage, Herts.

(1767)

**Science
group**
CIVIL SERVICE

THE NEWTON IN THE WILLOWS Trust, Northamptonshire. WARDEN-FIELD STUDY CENTRE. The Field Study Centre is due to open during 1974 to provide courses in a wide variety of subjects for schoolchildren, youths and adults. The Trustees wish to appoint a Warden with full academic and educational responsibilities for work at this Centre, at a salary on Local Government Scale—Senior Officer's grade (£2,820 to £3,165). Applicants should possess a good degree in an appropriate subject, preferably a teacher's certificate, and experience of teaching and organising Field Studies. Further details and application forms are available from the Secretary of the Trust at 9 Cheyne Walk, Northampton NN1 5PY. Closing date for applications: December 15, 1973. (1778)

UNIVERSITY OF EAST ANGLIA

Applications are invited for a

CHAIR IN BIOLOGY (ECOLOGY)

tenable in the School of Biological Sciences from October 1, 1974, or such other date as may be arranged. Candidates should have a special interest in animal ecology. This vacancy is due to the retirement of Professor J. A. Kitching, F.R.S.

Details from the Registrar and Secretary, University of East Anglia, Norwich, NOR 88C, with whom applications (one copy only) together with the names and addresses of three persons to whom reference may be made, should be lodged not later than December 31, 1973. (1753)

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL

(UNIVERSITY OF LONDON)

DENMARK HILL, LONDON SE5 8RX

SCIENCE GRADUATE, preferably with experience in tissue culture and/or cytogenetics, required to work as a Research Assistant in the Genetics Laboratory. The successful applicant will be expected to participate in a project concerned with the diagnosis of cancer. Salary according to age and experience.

Applications in writing with the names of two referees to the Secretary of the Medical School (N) not later than December 14, 1973. (1756)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS. AL5 2JQ

RESEARCH STATISTICIAN

to develop and exploit statistical techniques in agricultural science. Should be interested in programming and working on inter-disciplinary projects. Minimum qualifications: 1st or Upper 2nd class Honours Degree in Mathematics or Statistics and preferably post-graduate experience. Knowledge of agriculture or biology an advantage.

Appointment in grade of Scientific Officer (£1,590 to £2,177) or Higher Scientific Officer (£2,076 to £2,667) with a non-pensionable salary supplement of 41 per cent to offset F.S.S.U. contributions.

Applications naming two referees and quoting reference 2082 to the Secretary by December 21, 1973. (1808)

ROYAL VETERINARY COLLEGE

DEPARTMENT OF PATHOLOGY

VIROLOGIST

required urgently to expand a research group which is investigating the epidemiology, pathogenesis and immunology of virus infections in thoroughbred horses. The project is financed by a grant from the Horserace Betting Levy Board. Preference will be given to experienced applicants but recent graduates would be considered. There would be opportunities to study for a higher degree.

Salary in the Lecturer scale, up to £3,045 per annum including London Allowance: Superannuation under F.S.S.U.

Application forms and further details available from the Assistant Secretary (Personnel) (N), The Royal Veterinary College, Royal College Street, London NW1 0TU. (1805)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF ZOOLOGY AND
COMPARATIVE PHYSIOLOGY

A vacancy exists in the above Department for a Grade III RESEARCH TECHNICIAN to assist in research into neuro-transmission in sense organs. Some experience of electrophysiological and histological techniques would be desirable but not essential. Salary: £1,650 to £1,920 per annum.

Applications should be made to Assistant Secretary (Personnel), University of Birmingham, P.O. Box 363, Birmingham B15 2TT, quoting reference 141/B/968. (1810)

TECHNICIAN/GRADUATE to continue biochemical research in the Surgical Unit at St. Charles' Hospital, W10, and St. Mary's Hospital, W2. Initiative needed to work without direct supervision in the laboratory and ward. This interesting project is concerned with hormone release in vascular disease and is directed by a Consultant Surgeon. The salary is from £1,566 to £2,418 per annum, according to age

Veterinary Research

The Ministry of Agriculture, Fisheries and Food needs Research Officers in its veterinary laboratories at Weybridge and Shinfield. The main work of these laboratories is research into animal diseases and the means of dealing with them. They also carry out examinations in connection with scheduled diseases and official control schemes, and prepare certain biological products. Newly appointed Research Officers normally spend part of their first two years in training.

Central Veterinary Laboratory, Weybridge
In the Departments of Bacteriology, Biochemistry, Diseases of Breeding, Poultry and Virology.

Cattle Breeding Centre, Shinfield,
near Reading

For research into the biochemical and physiological aspects of bull and boar semen.

Appointment as Veterinary Research Officer Grade I (£3095-£3742) or Grade II (£2445-£3095). Starting salaries may be above the minima. Candidates must be members of the Royal College of Veterinary Surgeons. Preference will be given to candidates with post-graduate experience, and for appointment to Grade I level at least five years' relevant experience is required. There are prospects of promotion to posts carrying a salary of up to £6460 or higher.

For full details and an application form (to be returned by 28 December 1973) write to Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, or telephone BASINGSTOKE 29222 ext. 500 or LONDON 01-839 1992 (24 hour answering service) quoting S/8461/5.

(1829)

UNIVERSITY OF LEICESTER SCHOOL OF BIOLOGICAL SCIENCES ADMINISTRATIVE OFFICER

Applications are invited for the post of Administrative Officer in the School of Biological Sciences, which comprises departments of Biochemistry, Botany, Genetics, Physiology and Zoology. The Administrative Officer plays a central role in coordinating the teaching programme for the degree in Biological Sciences and in the provision of communal services and facilities, including workshops, illustration service, etc., in the School. The duties of the post include responsibility for the central administrative services of the School. Applicants should be graduates or have an appropriate professional qualification. The post would be suitable for a person with a background in science or technology. The appointment will be on the salary scale £1,804 to £3,336 per annum, initial salary will depend on age, qualifications and experience.

Further particulars and an application form can be obtained from: The Registrar, The University, Leicester, to whom completed applications should be forwarded by December 31, 1973. (1754)

UNIVERSITY OF LONDON READERSHIP IN BIOCHEMISTRY AT KING'S COLLEGE

The Senate invite applications for this newly established Readership. The appointment will date from April 1, 1974, or as soon as possible thereafter, and will be concerned especially with the teaching of medical students. Applicants should have active research interests, preferably in one of the following fields: bioenergetics, lipid or membrane biochemistry, enzymology, physical biochemistry. Salary scale: £4,368 to £5,496 a year plus £162 London Allowance.

Applications (10 copies) must be received not later than January 18, 1974, by the Academic Registrar (ND), University of London, Senate House, WC1E 7HU, from whom further particulars may be obtained. (1825)

UNIVERSITY OF MELBOURNE DEPUTY VICE-CHANCELLOR (RESEARCH)

The university is seeking a person with a distinguished career in research to fill the newly established post of Deputy Vice-Chancellor (Research). Interested persons are invited to inform the Vice-Chancellor before January 26, 1974. Additional information may be obtained from the Registrar, The University of Melbourne, Parkville, Victoria 3052, Australia. All correspondence should be marked "Confidential". (1734)

JUNIOR TECHNICIAN

required in the Department of Medicine to assist with research. Experience in radio-immunoassays an advantage, but not essential. Salary according to age and qualifications.

Apply in writing to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, quoting Ref. D.M.1. (1827)

CHARING CROSS HOSPITAL (FULHAM)

FULHAM PALACE ROAD, HAMMERSMITH, W.6
DEPARTMENT OF MEDICAL ONCOLOGY

POSTGRADUATE IN BIOLOGY required to work on immunological aspects (cell-mediated and humoral) of human cancer. Some knowledge of long-term tissue culture techniques would be an advantage. There will also be opportunities for the successful candidate to work for a higher degree.

Salary on scale £1,506-£2,643 (inclusive of London Weighting) according to qualifications and experience.

Please send curriculum vitae, with names and addresses of two referees, to Miss Matthews, Personnel Department, quoting Ref. 891. (1824)

UNIVERSITY OF PAPUA NEW GUINEA

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN MATHEMATICS OR STATISTICS. Appointee will be largely engaged in the teaching of Mathematics at pre-matriculation and elementary undergraduate levels, with a limited opportunity to lecture in more advanced courses. An interest in any branch of Pure Mathematics, Applied Mathematics or Statistics would be acceptable. Further information about the Department may be obtained by writing to Professor M. H. McKay.

Salary scales: (a) \$10,441 to \$12,089 per annum; (b) \$7,570 to \$10,205 per annum plus \$360 per annum dependants' allowance. These figures include an overseas allowance. (£1 sterling=\$1.60). Conditions include provision of housing, study leave, F.S.S.U.-type superannuation and annual leave fares. Applications (2 copies), should include particulars of age, marital status, academic record, qualifications and experience, the names and addresses of three referees, a recent small photograph and an indication of estimated starting date.

Further details and the conditions of appointment are available from K. R. Long, Secretary, P.O. Box 4820, University, Papua New Guinea. Closing date: January 18, 1974. (1788)

UNIVERSITY OF BRISTOL

Research Unit for Comparative Animal Respiration. RESEARCH TECHNICIAN Grade 5 required for work concerned with the physiology and ultrastructure of fish respiratory organs. Good knowledge of electronics particularly valuable. Previous experience in biological work, although desirable, is not essential. The successful applicant will be concerned with the design and construction of electronic apparatus used in the project. Salary in the range £2,007 to £2,382 per annum.

Applications, giving full particulars of qualifications and experience, together with the names of two referees, should be sent to Professor G. M. Hughes, Research Unit for Comparative Animal Respiration, The University, Woodland Road, Bristol BS8 1UG, as soon as possible. (1802)

ROYAL POSTGRADUATE MEDICAL SCHOOL

SENIOR TECHNICIAN (Histology) required to take charge of Histochemistry Laboratory mainly devoted to medical research. Duties include maintenance of equipment, performance of routine diagnostic histochemical reactions for muscle and other biopsies, and supervision of Junior Technicians.

Candidates should have a thorough knowledge of histological techniques and a desire to become acquainted with those of histochemistry. Salary according to qualifications and experience.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 6/201/N. (1762)

UNIVERSITY OF NEWCASTLE UPON TYNE DEPARTMENT OF PLANT BIOLOGY

Applications are invited for the post of JUNIOR RESEARCH ASSOCIATE (Salary scale £1,380 to £1,629) to work on the effects of antimony on plants. The post will be initially for one year but may be extended to three years.

Applicants should have an honours degree in a biological science and should have an interest in both the physiology and ecology of plants.

Applications, giving full particulars, including the names and addresses of two referees should be sent as soon as possible to: Dr D. J. Hill, Department of Plant Biology, University of Newcastle upon Tyne, Newcastle upon Tyne NE1 7RU. (1770)

Electron Microscopist

We are seeking the services of an experienced Graduate Electron Microscopist to join our Cell Biology Unit at Welwyn Garden City. The unit is based in recently completed research buildings where facilities and working conditions are excellent. The successful candidate will take full responsibility for running and maintaining our new Phillips 201 instrument and associated equipment, direct the work of a technician and report directly to the Head of the Unit. He will join an active group conducting original research into a variety of bio-medical fields including inflammation and tissue culture.

The person appointed will be in the 25-30 age range and have had two or three years post-graduate experience in microscopy. Familiarity with the methodology of cell culture and mammalian cell ultrastructure would be an advantage but are not essential.

For an application form and further information please apply in writing, quoting reference RG10, to the Personnel Officer at the following address.



Roche Products Limited
Welwyn Garden City Hertfordshire AL7 3AY

(1819)



ST. BARTHOLOMEW'S HOSPITAL
London EC1

POST DOCTORATE RESEARCH BIOCHEMIST

required in the Department of Medicine to work on Lipid Metabolism in human tissues. Salary according to experience.

Applications giving full details to Personnel Department quoting R/3798/N.

(1742)

INSTITUTE OF PSYCHIATRY DEPARTMENT OF BIOCHEMISTRY POST-DOCTORAL RESEARCH WORKER

Applications are invited for a Post-doctoral Worker, supported by the M.R.C., to study protein kinases and phosphoproteins in neural cell membranes in relation to the role of cyclic AMP in the brain. Salary within the range £2,091 to £2,385, appointment renewable annually up to 3 years.

Applications in writing (quoting reference RR/N), together with curriculum vitae, should be sent to the Secretary, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London SE5 8AF.

Applicants who wish to visit the Department may do so by prior arrangement. Telephone Dr R. Rodnight. 01-703 4411, extension 334. (1761)

SUNDERLAND POLYTECHNIC SCHOOL OF PHARMACY AND BIOLOGY BIOLOGY DIVISION

LECTURER GRADE I OR II IN GENETICS

Salary: Lecturer I £1,660 to £2,847
Lecturer II £2,515 to £3,243

Applications are invited for the above post from persons with a degree in a biological science and appropriate research/teaching experience in microbial or molecular genetics.

An application form and further particulars are available from the Personnel Officer, Sunderland Polytechnic, Chester Road, Sunderland SR1 3SD, and should be returned by December 14, 1973. (1747)

UNIVERSITY OF WESTERN AUSTRALIA PERTH

DEPARTMENT OF GEOGRAPHY

Applications are invited for the following appointments:

SENIOR LECTURER OR LECTURER from as early as possible in 1974. The appointee will be expected to conduct teaching and supervise research in the general area of his speciality as well as contribute to the general teaching programme of the Department. Candidates with interests in any field of geography will be considered, but preference will be given to those with interests in the broad field of environmental and cross field studies between human and physical geography, such as biogeography, land research, applied geography, applied geomorphology, anthropo-geography, resource investigation and planning Asian studies. An interest in collaborative work in first year courses and project orientated third year applied studies would be an advantage.

VISITING OR TEMPORARY LECTURER. Scholars seeking temporary sabbatical leave appointments in the following broad areas of specialisation—(a) climatology (preferably with biogeographical interests), (b) geomorphology (preferably with pedological interests) and (c) human geography (any field but preferably in areas of economic or spatial analysis)—are invited to write direct to the Head of the Department, Professor Martyn J. Webb. The appointments in physical geography would be for the 1974 academic year March to early October, and in human geography during the period August 1974 to July 1975. Applicants should state the period of their availability, lecturing fields and research interests. The fee for a visiting appointment would be negotiable.

SENIOR TUTOR-DEMONSTRATOR OR TUTOR-DEMONSTRATOR. Applicants should possess at least a good Honours degree in geography and preferably a postgraduate qualification. The appointee will be required to assist with teaching principally in first and second year courses in tutorials, practical classes, field work, maps, air-photo and quantitative methods. Candidates may have specialised in any field of geography but a real interest and concern for teaching is essential. The appointee will be able to undertake research for a higher degree by mutual arrangement with the Head of the Department.

Informal enquiries about all the above positions may be addressed to Professor Martyn Webb. The salary ranges are: Senior Lecturer—\$A12,268 to \$A14,308 per annum; Lecturer—\$A8,698 to \$A11,982 per annum; Senior Tutor—\$A7,270 to \$A8,698 per annum; Tutor—\$A5,740 to \$A7,015 per annum. Permanent conditions of appointment would include superannuation similar to F.S.S.U., fares to Perth for appointee and dependent family, removal allowance and housing loan scheme (not Tutors). A Senior Lecturer or Lecturer would be entitled to study leave and long-service leave, and a Senior Tutor to long service/study leave.

Applications in duplicate stating full personal particulars, qualifications and experience should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, by January 12, 1974. Candidates should request three referees to write immediately to the Staffing Officer. (1812)

UNIVERSITY OF QUEENSLAND AUSTRALIA

TUTOR IN BIOCHEMISTRY

To assist in the teaching in the laboratory classes in Biochemistry. Applicants should have at least a B.Sc. degree with a major in Biochemistry. In addition to teaching duties opportunity exists to carry out research and pursue a higher degree.

Salary: \$A5,332 to \$A7,015 per annum.

Additional information and application forms are obtainable from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in London and in Brisbane on December 7, 1973. (1814)

UNIVERSITY OF TORONTO DEPARTMENT OF PHYSICS

Applications are invited for a faculty position at the level of ASSISTANT PROFESSOR in the Department of Physics. Applicants should have a Ph.D. and research experience in solid earth physics. The solid earth physics group in the Department of Physics has an active and well supported research programme in geomagnetism, crustal seismology, tectonics and geochronology, and works in close co-operation with the Department of Geology. Appointment will be effective July 1, 1974.

Applicants should send curriculum vitae and names of three referees to: Professor D. J. Rowe, Department of Physics, University of Toronto, Toronto M5S 1A7, Ontario, Canada. (1813)

SENIOR TECHNICIAN

required to assist with the application of a variety of biochemical, immunochemical and histological techniques in studies of bone metabolism. Salary according to qualifications and research experience, within range £1,400 to £2,200 per annum. Applications in writing, with names of two referees, to Dr. M. Owen, Bone Research Laboratory, Churchill Hospital, Oxford OX3 7LJ. (1751)

UNIVERSITY OF HONG KONG LECTURESHIP/ASSISTANT LECTURESHIP IN BIOCHEMISTRY (NON-CLINICAL)

Applications are invited for appointment to the newly established post of Lecturer/Assistant Lecturer in Biochemistry in the Department of Medicine. Applicants must have a higher degree in Biochemistry and teaching and research experience, the latter preferably in clinical problems. The appointee will be required to participate in the teaching of biochemical aspects of disease to clinical undergraduates and in the research programme of the Department.

Annual salaries (superannuable) are:

Lecturer: HK\$40,800 by HK\$2,760 to HK\$46,320
BAR: HK\$49,080 by HK\$2,760 to HK\$56,400;
Assistant Lecturer: HK\$29,760 by HK\$2,760 to HK\$38,040. At the time of issue the rate of exchange is £1=HK\$12.15 approx.

Starting salary will depend on qualifications and experience. Salaries for female appointees below HK\$62,880 are slightly lower than given above; equalisation of male and female salary scales will be achieved by April 1, 1975.

Further particulars and application forms may be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF, or the Secretary to the Council, University of Hong Kong.

Closing date for applications is December 31, 1973. (1815)

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL University of London

Applications are invited for the post of
**DIRECTOR OF MULTI-DISCIPLINE
LABORATORIES**

This is an academic post providing good facilities and opportunities for research work in the Bio-medical field. The person appointed will be responsible for the management of the main teaching laboratories of the new medical school, which are due for completion in 1976. It is hoped to apply to the University for the conferment of title of Professor or Reader on the Director.

Salary plus responsibility allowances will not exceed £6,777 per annum.

For further particulars apply to the Dean, St. George's Hospital, Medical School, Blackshaw Road, London SW17 0QT.

Six copies of applications should be sent by January 4, 1974, quoting the names of 3 referees. (1817)

IMPERIAL COLLEGE LONDON SW7

Applications are invited for an Esso Bursary from those with a good honours degree in Physics, Chemistry, Chemical or Electrical Engineering for research into novel fuel burning devices including hybrid electrical combustion systems. The student appointed will be expected to register for M.Phil. and D.I.C. degrees and proceed to that of Ph.D. if suitable.

Application to Professor F. J. Weinberg, Department of Chemical Engineering and Chemical Technology, Imperial College, London SW7 2BY. (1801)

ZOOLOGIST ETHOLOGY LABORATORY. UFFCULME CLINIC, QUEENSBURIDGE ROAD, MOSELEY, BIRMINGHAM B13 8QD

Qualified Zoologist needed for the ethological study of human and sub-human primate behaviour.

Applications in writing to Group Personnel Manager, West Birmingham Hospital Management Committee, Box No. 293, Birmingham B18 7QH. Please quote Ref. 730/N. (1746)

FELLOWSHIPS AND STUDENTSHIPS

THE DENTAL SCHOOL, UNIVERSITY OF BIRMINGHAM. Applications are invited from graduates in Biochemistry or Chemistry for a **RESEARCH STUDENTSHIP** available in the Department of Oral Pathology in the Dental School. The project, which will be suitable for registration for a Ph.D., is on the subject of the composition and properties of the organic components of biological calcifications. The investigation will have particular reference to dental plaque and its mineralisation but a comparative approach involving study of microbial calcification and both normal and pathological calcifications is envisaged. No specialised dental background is required. Further details may be obtained from the Assistant Bursar, The Dental School, St. Chad's Queensway, Birmingham B4 6NN, to whom applications, including curriculum vitae and the names of three referees, should be sent by December 10, 1973. (1691)

AUSTRALIAN NATIONAL UNIVERSITY

Applications are invited for the following:

JOHN CURTIN SCHOOL OF MEDICAL RESEARCH

RESEARCH FELLOW IN BIOCHEMISTRY. Appointment will be in the Department of Biochemistry (Head: Professor F. W. E. Gibson, F.A.A.). The successful applicant will work within a group headed by Dr J. F. Morrison in continuing a research programme on the mechanism of action of multi-functional allosteric enzymes. Preference will be given to applicants who have had postdoctoral experience in the field of enzymology and who also are familiar with modern techniques of enzyme kinetics. Closing date: January 12, 1974.

SENIOR FELLOW IN IMMUNOLOGY. Appointment will be in the Department of Immunology (Head: Professor Bede Morris). Preference will be given to applicants who have worked in the fields of self-discrimination and immunological tolerance. Closing date: December 22, 1973.

Salaries: Salary on appointment will be in accordance with qualifications and experience within the ranges: Senior Fellow \$A14,308 to \$A16,462 per annum (6 by 359); Research Fellow \$A8,698 to \$A11,902 per annum (2 by 641; 2 by 640; 1 by 641).

Other conditions: Tenure: Senior Fellow for five years in the first instance with the possibility of extension to retiring age; Research Fellow normally for three years in the first instance with the possibility of extension to a maximum of five years.

Reasonable travel expenses are paid and assistance with housing is provided for an appointee from outside Canberra. Superannuation is on the F.S.S.U. pattern with supplementary benefits.

The University reserves the right not to make an appointment or to make an appointment by invitation at any time.

Further information should be obtained from the Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF. (1794)

UNIVERSITY OF WESTERN AUSTRALIA PERTH

Applications are invited for appointment as **RESEARCH FELLOW IN GEOLOGY (GEOCHRONOLOGY).**

DUTIES: Field, geochronological, and isotope geochemical studies associated with a research project dealing with the formation and evolution of Archaean crust in Western Australia. Further information on the project, which is sponsored by the Australian Research Grants Committee, may be obtained from Dr R. A. Blinn, University of Western Australia, or Dr J. R. de Laeter, Western Australian Institute of Technology (Hayman Road, Bentley, Western Australia, 6102).

QUALIFICATIONS: Ph.D. in geology or geochemistry, preferably with previous experience in mapping and Rb-Sr geochronology of granitic and metamorphic complexes. Training in laboratory techniques and instrumentation can be provided.

CONDITIONS: Salary range \$A8,698 to \$A11,982 per annum. The appointment will be for one year in the first instance, with probable renewal for a second year. Commencing date as soon as possible in 1974. An allowance towards fares will be provided for the appointee.

Applications in duplicate stating full personal particulars, qualifications and experience close with the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, on December 15, 1973. Candidates should request at least two referees to write immediately to the Staffing Officer. (1797)

SOMERVILLE COLLEGE OXFORD

The Governing Body of Somerville College, Oxford, invites applications from women graduates for a Mary Ewart Research Fellowship. The Fellowship will be tenable for two years from October 1, 1974, at an annual value of £750 together with free board and residence in college. Selected candidates will be asked to attend for interview.

Particulars and application forms may be obtained from the Secretary to the Mary Ewart Trustees, to whom applications should be sent by January 21, 1974. (1768)

THE UNIVERSITY OF MANCHESTER SIR HENRY ROYCE FELLOWSHIP FOR RESEARCH IN RHEUMATISM

Applications invited for this Fellowship for research into the causes and possible cure of rheumatism and allied diseases. Postdoctoral applicants interested in the biochemistry of collagen or in organ culture of synovia preferred. The Fellow would work as part of a team studying abnormalities of synovial membranes in rheumatoid arthritis and other arthritides. The Fellowship, which is tenable for three years, is valued within the range £1,929 to £2,718 per annum. F.S.S.U.

Further particulars and application forms (returnable by December 8) from the Registrar, The University, Manchester M13 9PL. Quote ref.: 208/73/Na. (1661)

BEIT MEMORIAL FELLOWSHIPS FOR MEDICAL RESEARCH—1974

Notice is hereby given that an election of Junior Fellows to begin work on October 1, 1974, will take place in May 1974. Junior Fellows have annual values within the range of £1,750 to £2,220 per annum, plus yearly increments of £150 for 3 years. As a rule, superannuation benefits are provided, to which the successful candidate will be required to contribute 5 per cent of the annual stipend and to which the Trust will make a contribution of 10 per cent. Candidates must have taken a degree in a faculty of a university approved by the Trustees in Her Majesty's Dominions, Protectorates and Mandated Territories, India, Pakistan, the Republic of Ireland and the United Kingdom, or a medical diploma registrable in the U.K. Elections to Junior Fellowships are rarely made above the age of 35 years. Applications from candidates must be received not later than March 22, 1974. Candidates must submit evidence that they can be given accommodation in the departments where they propose to work, which must be in Great Britain or Ireland.

Forms of application and all information may be obtained from Professor W. S. Spector, Pathology Department, St. Bartholomew's Hospital, London EC1A 7BE. For overseas candidates forms of application may be obtained from the Secretary, South African Medical Council, P.O. Box 205, Pretoria, South Africa; The Ministry of Health, The Government of India, New Delhi, India; the Secretary, Department of Education and Science, P.O. Box 826, Canberra City, A.C.T. 2601, Australia; The Department of Health, Wellington, New Zealand; and The Canadian Medical Association, 1867 Alta Vista Drive, Ottawa 8, Ontario, Canada. (1743)

UNIVERSITY OF LONDON

BRITISH POSTGRADUATE MEDICAL
FEDERATION
INSTITUTE OF LARYNGOLOGY AND OTOTOLOGY
330/336 GRAY'S INN ROAD, LONDON WC1

BERNARD SUNLEY RESEARCH FELLOWSHIP

Research Fellow in electron microscopy required for investigation of inner ear, grant-aided for a term of 3 years, which could be suitable for a term. Should be graduate in Biology, with some E.M. experience. Salary £2,241 rising to £2,559.

Applications with full curriculum and naming referees to the Secretary-Administrator, Institute of Laryngology and Otology, 330/336 Gray's Inn Road, London, W.C.1. (1684)

LA TROBE UNIVERSITY MELBOURNE, AUSTRALIA

LECTURER/RESEARCH FELLOW (POSSIBLY TWO POSITIONS) GENETICS AND HUMAN VARIATION

Applicants will be qualified in any field of the discipline, but a person with interest in human or animal genetics may be given preference for one position. A Research Fellow can expect a two-year appointment. In exceptional circumstances the appointment may be made at Senior Lecturer level. Information may be obtained from Professor P. A. Parsons, Chairman of the Department in the University. Salaries: Senior Lecturer, \$A12,268 by \$A408 (5) to \$A14,308; Lecturer, \$A8,698 by \$A470 (1) by \$A469 (6) to \$A11,982; Research Fellow, \$A8,128 by \$A285 (6) to \$A9,838 (tentative).

Further information and application forms are available from the Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF, or from the Registrar, La Trobe University, Bundoora, Victoria, Australia 3083. Applications close on January 31, 1974. (1799)

UNIVERSITY OF WESTERN AUSTRALIA PERTH

RESEARCH FELLOWSHIPS

A limited number of Research Fellowships will be offered to be taken up as early as possible in 1974. Appointment will be for one year in the first instance with the possibility of annual renewal for up to a further two years. The Fellowships will be tenable in any academic department and are intended primarily for Ph.D. graduates (normally from other universities), or those with equivalent qualifications, who by publication and in other ways have demonstrated significant research capability. Salary will be within the range \$A7,270 to \$A8,698 per annum and appointees may in certain circumstances be considered for admission to an F.S.S.U. type superannuation scheme. Fellows may be given the opportunity to participate in teaching.

Prospective applicants should write in the first instance to the head of the appropriate academic department describing their field of research interest and setting out their qualifications and publications. Those then invited by the Head of Department to submit a formal application should do so to the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, by January 12, 1974.

DALHOUSIE UNIVERSITY
HALIFAX, NOVA SCOTIA, CANADA

The Izaak Walton Killam Postdoctoral Fellowships 1974-75

VALUE

Fellowships valued at \$8,800, plus travel allowances, are tenable for one year at Dalhousie University in most fields of study. Applications for extensions may be considered.

QUALIFICATIONS

Applicants should not be more than thirty-five years of age and should possess a Ph.D. degree from a recognised university, or expect to obtain a degree before taking up an award. Fellows may engage in teaching or other similar duties in the University.

APPLICATION

Application forms may be obtained by writing to: The Office of the Dean, Faculty of Graduate Studies, Dalhousie University, Halifax, Nova Scotia, Canada.

The Izaak Walton Killam Fund for Advanced Study at Dalhousie University was founded by Mrs Dorothy J. Killam in memory of her husband Izaak Walton Killam. Her purpose was to establish a perpetual memorial to her husband in his native province and "to help in the building of Canada's future by encouraging advanced study".

Please quote code **X323** in your application.

(1730)

European Molecular Biology Organization (EMBO)

Short- and long-term fellowships in molecular biology

The European Molecular Biology Organization intends to award to scientists working in laboratories within the European area both short-term (from a few days to several weeks) and longer-term fellowships for collaborative research or advanced training in molecular biology.

The Short-term Fellowships are to support visits to other laboratories for the purpose of carrying out experiments with special techniques or of other forms of scientific collaboration or advanced training, and especially to support developments arising at short notice.

The Long-term Fellowships will usually be for a period of one year, but applications for renewal will be considered. They will be awarded upon individual application, at the "junior" level to promising young research workers who may then spend prolonged periods in other laboratories working under the guidance of leaders in the field of molecular biology. At the "senior" level, they may be awarded to enable established research workers to gain experience in new approaches and new problems. Upon application by European Institutions fellowships at the "senior" level may also be awarded to specialists who can assist in the initiation and development of research programmes in the sponsoring Institution. Such "sponsored" awards may be made to established workers at all stages of their career beyond the postdoctoral stage.

Application forms and further details may be obtained from Dr. J. Tooze, Executive Secretary, European Molecular Biology Organization, 6900 Heidelberg 1, Postfach 2029 (Postfach 1022.40 after July 1, 1974), Germany.

Application for Short-term Fellowships may be made at any time and will be decided upon soon after receipt of the application. Applications for Long-term Fellowships should be made before February 1 for a decision by April 30 and before August 1 for a decision before October 31. Because the selection procedure involves an interview these deadlines for application should be respected.

(X1822)

UNIVERSITY OF ABERDEEN DEPARTMENTAL STUDENTSHIP IN ZOOLOGY

Applications are invited for above Studentship from February 1, 1974. The Studentship is valued at £695 per annum plus demonstrating fees and dependants' allowances where appropriate. The successful applicant will be expected to take part in a continuing research project on population ecology of the rook, based at Culterty Field Station, Newburgh. Further particulars from the Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by December 15, 1973. (1769)

MONASH UNIVERSITY DEPARTMENT OF PSYCHOLOGY RESEARCH FELLOW/SENIOR RESEARCH FELLOW TO STUDY ROAD USER BEHAVIOUR

Applications are invited for appointment as Research Fellow or Senior Research Fellow to join a group undertaking a three-year research programme funded by the Australian Department of Transport on road user behaviour as it relates to accidents.

Applicants will be expected to have higher degree qualifications in psychology, human factors engineering, traffic engineering, epidemiology or some other appropriate discipline, and to be experienced in applied research in human behaviour.

Salary: Research Fellow, \$A7,627 to \$A11,982 per annum; Senior Research Fellow, \$A12,268 to \$A15,940 with superannuation based on an endowment assurance scheme, the employee and employer contributing 5 per cent and 10 per cent respectively. The appointment will be for a period of three years.

Benefits: Travelling expenses for appointee and family; removal allowance; temporary housing for an initial period. Repatriation after three years' service if desired.

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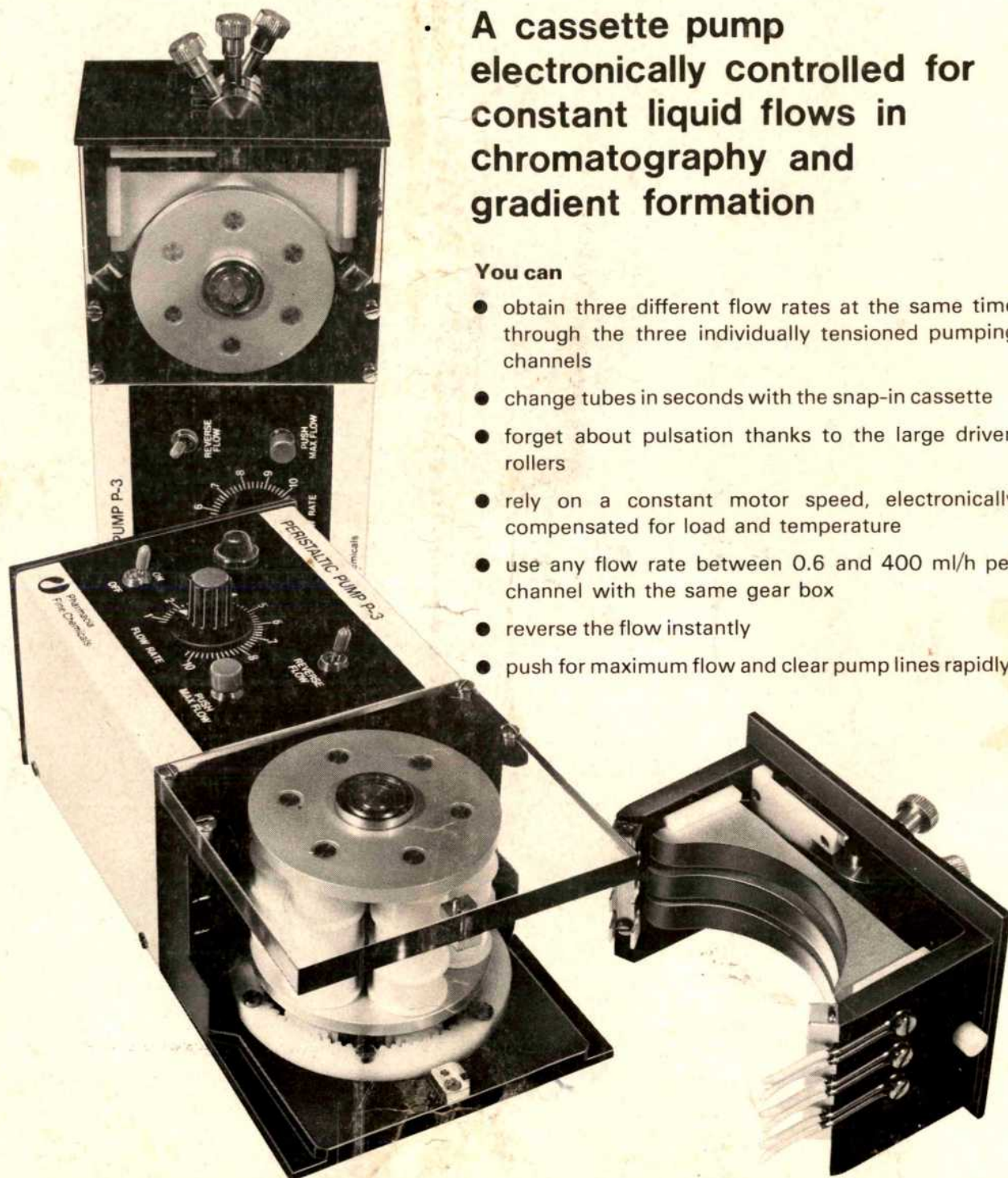
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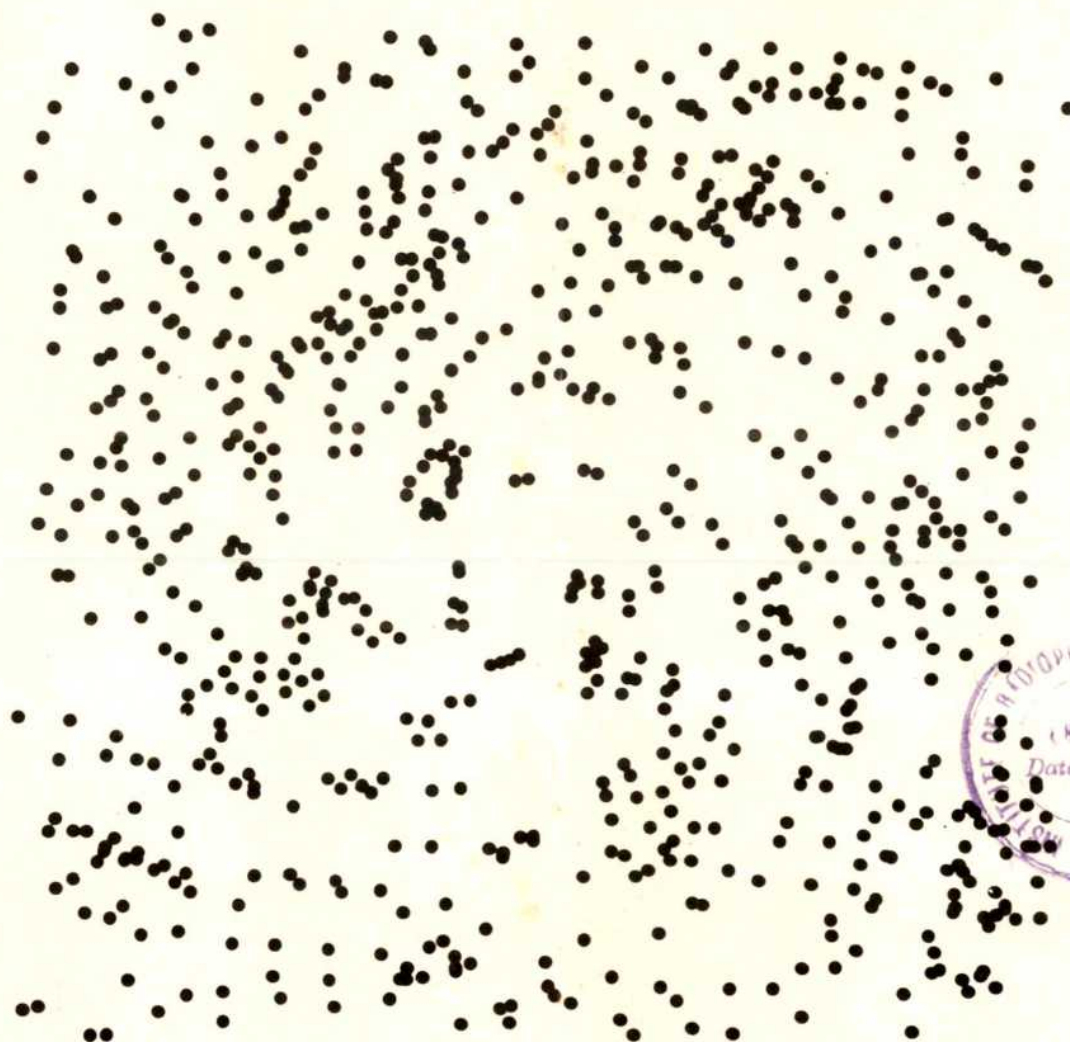
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FRIDAY



Pattern perception

Search for gravitational radiation

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by M. I. BUDYKO

edited by DAVID H. MILLER

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1973, about 579 pp., in preparation

TOPICS IN RADIATION DOSIMETRY

Supplement 1/Radiation Dosimetry

edited by FRANK H. ATTIX

CONTENTS: M. J. AITKEN and S. J. FLEMING: Thermoluminescence Dosimetry in Archaeological Dating. K. BECKER: Dosimetric Applications of Track Etching. T. E. BURLIN: Vacuum Chambers for Radiation Measurement. W. A. GLASS and W. A. GROSS: Wall-Less Detectors in Microdosimetry. J. R. GREENING: Dosimetry of Low Energy X Rays. R. KATZ, S. C. SHARMA, and M. HOMAYOONFAR: The Structure of Particle Tracks. D. NACHTIGALL and G. BURGER: Dose Equivalent Determinations in Neutron Fields by Means of Moderator Techniques. E. PIESCH: Developments in Radiophotoluminescence. APPENDIX: Useful Physical Constants and Conversion Factors.

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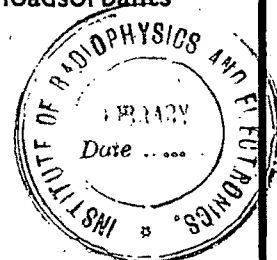
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	Page		Page
Challenge to Scientists	321	Anellotubulates—Artefacts of sample preparation procedure—RICHARDSON, GREGORY (Institute of Geological Sciences, Leeds) and POLLARD (Manchester)	347
The Problem of Soviet Scientists	322	Oceanography—Flocculation of suspended sediment in the sea—KRANCK (Bedford Institute of Oceanography, Dartmouth, Nova Scotia)	348
NEWS			
Oil from Shale: Answer to the Energy Crisis ?/Nuclear Power/Air Pollution/Copyright/Energy/Short Notes	323	Biological Sciences	
NEWS AND VIEWS			
A Better Future for ISC ?/T Lymphocytes in Nude Mice ?/ Probing Lunar Carbon/Troponin/Juvenile Hormone/ Cancer Research/Pesticides/Iron-Sulphur Proteins/ Space Research/Earthquake Prediction/Materials/ Nuclear Theory	327	Lymphocytes— θ -bearing lymphocytes in nude mice—RAFF (University College London)	350
ARTICLES			
The Individual and the Information Problem—BLAXTER (Rowett Research Institute) and BLAXTER (Aberdeen)	335	Histocompatibility antigens—Recognition of T cell function—RAMSEIER (Zürich)	351
Gravitational radiation—Unsuccessful search for pulses —DREVER, HOUGH, BLAND and LESSNOFF (Glasgow)	340	Glucocorticoid receptors—Differences between cytoplasmic glucocorticoid-binding proteins shown by heterogeneity of nuclear acceptor sites—LIPPMAN and THOMPSON (NIH, Bethesda)	352
LETTERS TO NATURE			
Physical Sciences			
Atmosphere—Observations of potassium by laser radar —FELIX, KEENLISIDE, KENT (West Indies, Jamaica) and SANDFORD (SRC Appleton Laboratory, Slough)	345	Heparin—A generalised view of its anticoagulant action —DAMUS, HICKS and ROSENBERG (Beth Israel Hospital and Harvard Medical School)	355
Tidal friction—New estimate—JEFFREYS (Cambridge)	346	Insect vision—Perception of polarised light—GRIBAKIN (Leningrad)	357
		Vision—Alteration of visual cortex from environmental asymmetries—FREEMAN and PETTIGREW (California, Berkeley)	359
		—Perception of random dot interference patterns —GLASS and PÉREZ (Rochester, New York)	360

Notes of articles appearing next week in *Nature Physical Science* and *Nature New Biology* will be found on pages 331 to 333.

(Continued overleaf)

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1971, xviii, 493 pp.
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Volume II begins with certain expository material in infinite dimensional manifolds, Lie algebra theory, and algebraic topology, and proceeds to describe how the basic formalism of vector bundles and differential operators on manifolds may be used in quantum mechanics, quantum field theory, group representation, and Lie algebra theory. 1970, x, 400 pp.,

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ADVANCED BOOK PROGRAM

	Page		Page
BOOK REVIEWS			
The Special Theory of Relativity, H. Muirhead (W. H. McCREA)	363	Biology of <i>Hydra</i> , Allison L. Burnett (editor) (GERALD WEBSTER)	365
Explorers of the Brain, Leonard A. Stevens (J. C. ECCLES)	363	Patterns of Change in Graduate Employment, H. Greenaway and G. Williams (editors) (B. J. HOLLOWAY)	365
Early Human Development, S. J. Hutt and Corrinne Hutt (editors) (S. A. BARNETT)	364	Ectomycorrhizae, G. C. Marks and T. T. Kozlowski (editors) (B. W. FERRY)	366
A Sadly Mismanaged Affair: Political History of the Third London Airport, David McKie (D. DAVIES)	364	Attention and Performance IV, Sylvan Kornblum (editor) (DONALD E. BROADBENT)	366
Bacterial Plasmids: Conjugation, Colicinogeny, and Transmissible Drug-Resistance, G. G. Meynell (N. S. WILLETTTS)	364	Obituary—Selman Abraham Waksman	367
		Announcements—University News/Miscellaneous	368

Next Monday's issue will include

- Her X-1**—Model for the 35-d periodicity—KATZ (Cornell)
- Magnetic fields**—Possible origin in neutron stars and white dwarfs—RUDERMAN and SUTHERLAND (Columbia)
- Magnetosphere**—Type IPDP plasma wave events—HEACOCK (Alaska)
- Radio Source 0048-097**—New results—CARSWELL, STRITT-MATTER (Arizona), DISNEY (ANU), HOSKINS and MURDOCH (Sydney)

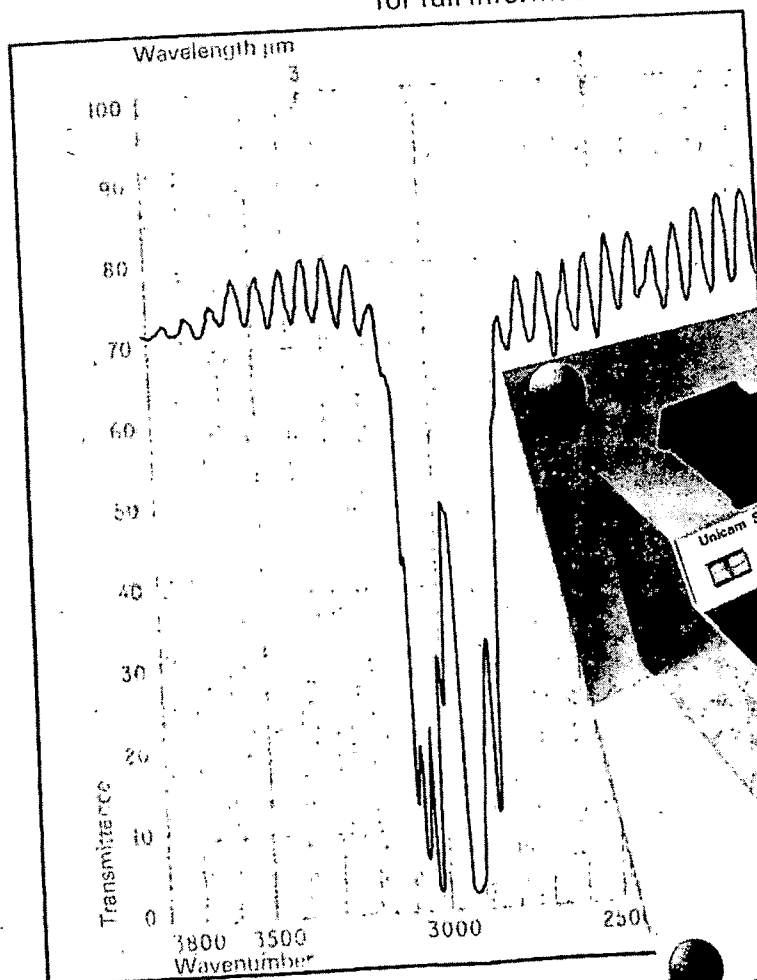
Next Wednesday's issue will include

- Nucleic acid structure**—X-ray study of helix, loop and base pair stacking in trinucleoside diphosphate ApApA—SUCK, MANOR, GERMAIN, SCHWALBE, WEIMANN and SAENGER (Max-Planck, Göttingen)
- Transfer RNA**—Structural studies on a tyrosine tRNA precursor—CHANG and SMITH (MRC Molecular Biology, Cambridge)
- Pineal hormones**—Arginine vasotocin release into cerebrospinal fluid of cats induced by melatonin—PAVEL (Institute of Endocrinology, Bucharest)
- Haemoglobin**—Hereditary persistence of foetal haemoglobin associated with a $\gamma\beta$ fusion variant, haemoglobin Kenya—SMITH (MRC Project, Kisumu), CLEGG, WEATHERALL and GILLES (Liverpool)

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Challenge to Scientists

BRITAIN has recently been experiencing the strange happenings that seem to accompany Mr Uri Geller wherever he takes his one-man show. Knives and forks have been bent, broken watches restarted and feats of apparent telepathy performed. No generally accepted explanation is yet forthcoming.

Although the phenomenon of Mr Geller is new to Britain, he is well known both in Israel and the United States for his performances. It is important that he claims to be doing these strange things not as an illusionist using sleight of hand or deceptive material but as someone invested with a previously unappreciated power. He is prepared to back up this claim very convincingly by performing in such inauspicious surroundings as the back of a taxi in the company of the Science Correspondent of the *Sunday Times*. If he is an illusionist he runs the risk of being detected every time he shows off his skills, particularly when his performance goes on to videotape. Further, any stagehand knows how an illusionist works, but none has yet revealed Mr Geller's secrets.

It needs to be said, however, that not everyone is convinced that Mr Geller is other than a great illusionist and that there seems to be somewhat more scepticism in Israel and the United States than has yet developed in Britain. For a fairly cool assessment *Time* of March 12, 1973, should be read. Nevertheless he has clearly created a *prima facie* case for further investigation and it is to be hoped that the proposal by the *New Scientist* that he submit to examination by its panel will be taken up, even though he has already been examined extensively by a team at Stanford Research Institute.

What does all this mean for the scientist—and not necessarily only the scientist interested in psychic research? There are two distinct challenges to him.

The first is that analysis of this phenomenon must be absolutely neutral and above board. One of the remarkable things about this whole affair has been the way the public has asked that it be investigated by scientists. It has been common to hear phrases such as "I will not be happy until a panel of scientists have pronounced on it". In mediaeval times it was priests, later it was noblemen, in Victorian times businessmen and now scientists who are the arbiters of acceptability and correctness. It is not possible to believe that this situation will last much longer though it is difficult to decide who will eventually supplant the scientist in this role—trade unionist, professional footballer or television announcer. Nevertheless, while this duty still falls to the scientist he has a great responsibility to be utterly objective and entirely open. There have been some doubts cast on the Stanford investigation because of the lack of publication of the results apart from a report at a conference. On the other hand it is undesirable that Mr Geller should be used either by someone delighting in the occult or exceedingly sceptical of it.

The second challenge to scientists will arise if investigations continue to turn up signs of psycho-kinetic powers, and with the present evidence this certainly cannot be ruled out. It would then be urgently necessary for the

scientific community to come to terms with something totally beyond its powers of explanation—indeed something which in a religious context would be called a miracle. Just as the public wants scientists to validate Mr Geller, it would also want them to explain him and, however awkward this question may be, it should not be avoided. If Mr Geller indeed possesses extraordinary abilities it is immaterial whether he is an isolated unrepeatable phenomenon or whether a large number of people can be taught the skills; and it is immaterial that he manifests the abilities in ways up to now better known to music-hall illusionists than to scientific investigators. The challenge would still exist—that well established scientific laws as apparent to laymen as to scientists are not inviolate under the influence of some presumed mental process.

It is difficult to see how research into the causes of such extraordinary happenings could proceed. One suspects that any approach which involved extensive instrumentation would end unsuccessfully. Technology has an unerring ability to suppress human skills. Nevertheless a boost for psychical research would be very welcome. There are too many loose ends lying around for comfort, and psychical research has not yet been able to shake off its mildly eccentric character and its ability to attract fierce criticism.

The viewing public, shown a chest operation under acupuncture one week and an exhibition of knife bending the next, is bound to ask searching questions about conventional scientific wisdom.

100 Years Ago



THE London Association of Correctors of the Press held a *conversazione* on Saturday last under the presidency of Mr. B. H. Cowper, editor of the *Queen*. We are glad to notice that the principal items of the programme were of a scientific character. Mr. E. R. Johnson, Chairman of the Association, read a paper on the past work of the Association, enumerating some of the papers and discussions on philological topics which had engaged its attention, and while commending the study of philology, the advantage of an acquaintance with one or other of the exact sciences was set forth. Mr. G. Chaloner, late Secretary of the Association, and lecturer on Chemistry at the Birkbeck Institution, enlightened the meeting as to some of the properties of hydrogen, accompanying his remarks with appropriate experiments. Mr. J. T. Young discoursed on the glacial period, and exhibited some fossils illustrative thereof. The wonders of the microscope and stereoscope also contributed to the enjoyment of the evening.

From *Nature*, 9, 114, December 11, 1873.

The Problem of Soviet Scientists

Professor John Ziman of the University of Bristol puts forward views on the need for scientific institutions not to acquiesce in any Soviet policy of repression of scientists.

MUCH of the concern amongst Western scientists about the situation of their Russian contemporaries arises from humanitarian, ideological or political motives. By our standards, life in the Soviet Union seems uncomfortable, inequitable, and constrained. But there are worse institutions in the world to protest against than the Soviet government; and by comparison with many of their fellow citizens Soviet scientists are relatively privileged. Andrei Sakharov and other political dissidents are brave men who deserve every sympathy; but the cause of freedom and humanity has many other heroes. The treatment of Jewish scientists and intellectuals seeking to emigrate to Israel is deplorable; but to some extent they bring this on themselves. It is a gross professional abuse of psychiatry to pretend that a prison is a mental hospital; but not so brutal as the police torture that disgraces many other states that pretend to adhere to the principles of the United Nations. In other words, although we may each, individually, give more or less weight to a variety of such factors, the state of Soviet science does not necessarily have the first claim on our humanitarian sympathies and moral indignation. In any case, action based on such motives does not lie within the competence of professional scientific organs such as learned societies and learned journals.

Soviet Science a Part of World Science

There remains, nevertheless, a central feature which makes this our business as scientists. Soviet science is not an independent national institution: it is an integral part of world science. Having made personal contact with our opposite numbers behind the Iron Curtain, we are obliged to help them when they are in trouble. Having shared in the pursuit of the same scientific goals, we cannot be indifferent to the disabilities under which their research is carried out. Since every scientist relies upon the skill and integrity of all the other scientists whose work he cites, it is a matter of the utmost concern to every non-Soviet scientist

that Soviet science should be of the highest quality: it would be very damaging to our own research if this significant fraction of the total world scientific effort were to fall into decay and disrepute.

From the Soviet point of view, also, much of their immense expenditure on science would be wasted if it were not up to the highest international standards. These can only be maintained by a vigorous internal climate of scientific criticism and open access to the world stock of scientific information. To achieve this, it is evidently in the Russian interest to draw in as many scientific conferences and scientific visitors as they can. But membership of this valuable club implies reciprocal courtesies and obligations. In return for such trouble as we may take in travelling to the Soviet Union, we may reasonably request that Soviet scientists participate fully in conferences in our own countries, and give freely of their scientific learning in visits to our own universities and laboratories. Severe restrictions on foreign travel by Soviet scientists are not only harmful to science in Russia: they are harmful and offensive to the whole international scientific community.

Even more serious is the evidence that attempts are being made by the Soviet authorities to violate the recognised norms of the scientific profession. It is essential to the intellectual integrity of science that due recognition be given for published work that makes a significant contribution to knowledge. Such high recognition as election to a national scientific academy is understood throughout the world as the reward for outstanding scientific achievement, measured according to the universal standards of international science. The Soviet Academy of Sciences is rightly regarded as one of the most distinguished bodies of this kind. Yet we hear of threats of expulsion against members of the Soviet Academy as 'punishment' for legal acts such as expressing dissident opinions or asking for permission to emigrate to Israel. If the Soviet Academy were to agree to act thus it would forfeit its position as a

leading institution of the world of science.

However much we may deplore it, we cannot insist that the sanction of dismissal from employment should not be used by Russian state organisations against scientists who are in political disfavour: membership of the Invisible Colleges of the international scientific community is not a guarantee of a well paid job for life. But further actions such as shutting dismissed scientists out of international conferences held in the Soviet Union, withdrawing their books from scientific libraries, and ordering that their previous published work should not be cited by other Russian scientists, are inadmissible. It must be emphasised that these vindictive procedures are being taken against Soviet citizens who have not been convicted of any criminal offence, but who have, on the contrary, earned their scientific reputation by hard honest labour over many years. The consequences of such a policy can only be the degradation of intellectual standards in Soviet science, and its further alienation from the world scientific community.

Scientific Standards Threatened?

These issues are so serious, and touch so deeply the whole practice and professional ethos of science, that we must not remain indifferent to them. The Soviet Union is not a banana republic making an insignificant contribution to science: it is a Super Power, whose brilliant scholars and immense laboratories play a major part in the advancement of knowledge. Not only the content, but also the style of scientific research throughout the world in the next few decades will owe a great deal to the way in which science is being done now in such great nations. It is evident that the Soviet government does not understand the delicate social structure of the Republic of Science, and persists in treating its scientific workers and scientific institutions as entirely subservient to immediate national political ends. Whilst insisting on the right to partake fully of the products of research, it is undermining the system that makes these products reliable and valuable. Unfortunately, this sort of short-sighted policy comes all too easily into the calculations of any power-hungry bureaucratic authority, whether nominally socialist or nominally capitalist. If we

acquiesce now in this particular subversion of the moral principles of the scientific profession, then in the long run we may bear the responsibility for the decadence of our own science at the hands of politicians, administrators, and other gentle experts in the arts of expediency.

Much can be done by individual protests and boycotts. But the responsibility for the protection of the norms of science rests squarely on the great learned societies, led in Britain by the Royal Society. If they fail in this duty, then who else could be blamed for inaction? What has prevented the Royal Society from speaking up in defence of the scientific ethos which it is pledged to preserve?

On the one hand, there are a few leading British scientists who hold that any criticism of Russian scientific policy is a political act motivated by disreputable ideological ends. On the other hand, there are administrative 'realists' who have no illusions about the disabilities of Soviet scientists, but who insist that more can be achieved by secret diplomacy than by open comment. These two extreme parties combine to prevent the whole subject from being properly discussed. For opposite reasons they express themselves strongly against any action, and thus paralyse the large middle body who feel uneasy about the situation but who have no great personal interest in upsetting the *status quo* of acquiescence. It is to the conscience of this group that my argument is addressed.

The most important and decisive action would be public recognition by

the Council of the Royal Society of the main facts concerning the state of science in the Soviet Union, and an expression of support for the basic principles of academic freedom and integrity. Whatever might be the overt reaction of the administrative organs of the Soviet Academy of Sciences, such a statement would make it quite clear to the main body of Russian scientists that we understand their present position and sympathise with their personal endeavours to contribute honestly to the world stock of human knowledge. In the absence of such a public statement, claims of influence by secret bargaining are without weight; the very fact that various officers of the Royal Society deal directly with the officials of the Soviet Academy can only suggest to other Russian scientists that they are ignorant of, acquiesce in, or even approve the corruptions with which we are here concerned.

Exchanges of Scientists

It is often suggested, both by Soviet apologists and by official 'realists', that the channels of communication must be kept open. They point, for example, to the Scientific Exchange agreements by which visits are arranged between the Soviet Union and other countries. In all honesty, however, it must be admitted that these exchanges are of such insignificant proportions that their value is negligible. The number of Russian scientists that visit Britain under such schemes is probably about the same as the number of Israeli or Australian scientists who come and talk with their

British colleagues. The truth is, also, that many of the present Russian visitors to the West are of very low scientific standing, and are apparently more competent at picking up snippets of information than communicating at the highest intellectual level with our own leading scholars. The average Soviet scientist of good repute has so little expectation of making a foreign visit himself that he would not be greatly perturbed if those particular exchanges were inhibited!

In any case, the flow along these channels is controlled almost entirely by the Soviet authorities themselves. It is not suggested that the Royal Society, the British Council, or other agencies should act in any other way than to welcome exchange visits by *bona fide* scientists. If Soviet officialdom were to react to criticism of their domestic policies by refusing to collaborate in such exchanges, the responsibility would be theirs. What sort of a bargain is being struck when one promises silence in return for an agreement that mainly benefits the other party?

And that is the heart of the matter. The present efforts of the Soviet government in the scientific and intellectual sphere seem directed with pathological intensity towards suppressing all internal criticism. For all the talk of *détente*—an issue which lies of course in the political sphere and therefore outside the competence of our scientific institutions—it would be tragic folly if we also were coaxed into silence about the injustices being done to our scientific colleagues and friends in that great country.

NEWS

Oil from Shale: Answer to the Energy Crisis?

by our Washington Correspondent

BENEATH a remote region of the Rocky Mountains lies a band of rock which contains enough shale oil to dwarf all the other United States domestic reserves of petroleum put together. Some 1,800 billion (US) barrels of oil are locked into the rock there, and up to a third of it is in deposits rich enough to be exploited commercially. Last week, the federal government took the first tentative step towards developing the resource, for Rogers C. B. Morton, Secretary of the Interior, announced that six tracts of federal land will be leased to oil companies next year so that they can begin producing shale oil

Unfortunately, however, the sheer magnitude of the deposits has led to some unfounded optimism and grossly overstated predictions about the potential impact of shale oil production on fuel supplies in the United States. There are many problems ahead for those intent on developing the resource and there are factors which are likely to set physical limits on the rate at which shale oil will be produced. Thus shale oil is unlikely to provide salvation from the energy crisis, as some have predicted. But one thing is certain: the emergence of a shale oil industry will radically alter a large area of Colorado, Wyoming and Utah, and it will cause massive destruction of the environment.

The leases announced last week will

allow a prototype operation to get under way and the objective is, on the one hand, to enable the oil companies to test the technology for producing oil from shale on a moderately large scale and, on the other, to enable the Department of the Interior to take stock of the environmental damage that results. After three or four years, the companies should be able to decide whether oil shale development is commercially attractive and the federal government will be able to decide whether the environmental costs justify throwing the whole area open for development.

The six tracts to be leased next year—two each in Colorado, Utah and Wyoming—cover a combined area of some 30,000 acres; the entire oil shale

field spans some 25,000 square miles. That is an area equal in size to the state of West Virginia or three times the size of Wales. Most of the land is owned by the federal government, which is thus in a position to dictate the pace and scope of development.

It has been known for a long time that huge quantities of shale oil lie under part of the Rockies and, in fact, some oil was produced from shale deposits before natural petroleum was discovered in 1859. But the cost of extracting oil from the shale has always made it commercially unattractive—at least until the energy crisis caused the costs of other energy supplies to increase. And the Arab oil producers have now turned out to be the best friend that potential oil shale producers could possibly have, for their embargo on oil exports to the United States has turned the shale fields into a goldmine almost overnight.

Shale oil is locked into rock in the form of a solid hydrocarbon called kerogen. To get it out requires the rock to be heated to about 900° F and the gases and petroleum vapours that boil off collected. Potential oil shale producers have been experimenting for several years with two different approaches to that deceptively simple task. One involves mining the shale, crushing it and heating it in a retort. The other involves either blasting or excavating a cavern beneath the surface, burning gases in the cavern to cause oil to flow out of the surrounding rocks and pumping the products to the surface. The former approach has received the most attention and will probably be the one adopted by most of the companies that will be bidding for the leases next year.

This is how the process will work. Oil shale will be mined either by open-pit mining where it is close to the surface—only a small area of the Colorado shale fields will be surface mined—or by the simple room-and-pillar method. It will then be crushed into marble-sized pieces and fed into a retort which will initially be capable of processing up to 10,000 tons of shale a day. Several different designs of retort have been patented, and they involve heating the shale either by burning some of the oil in the rock or burning some of the gases produced from the shale. One process also involves heating ceramic balls in a separate plant and using them to retort the shale. In any case, the resulting product is a viscous, low gravity, moderate-sulphur and high-nitrogen oil.

Once the oil and gases have been extracted from the shale, the problem is then what to do with the vast quantities of rock left over. The crushing and retorting process expands the rock considerably, so it cannot be simply fed back into the mines, and the only solution will be to dump it into canyons and to build up new slopes which will then

have to be revegetated. The oil shale region will thus experience something of a transformation.

The Department of the Interior reckons that the prototype operations will eventually lead to the production of some 250,000 barrels of shale oil a day and that, if full commercial development of the shale fields proves to be acceptable, 1 million barrels of oil could be produced by 1985. A simple calculation shows, however, that such a programme would be a massive undertaking, which, for a variety of reasons, may be close to the limit of production capabilities.

The sheer scale of such an operation is one stumbling block. It is reckoned that to be commercially attractive to exploit, the shale will have to contain at least 25 gallons of oil per ton of rock. Thus, for every barrel of oil produced (one barrel is 42 US gallons) two tons of rock will have to be processed and dumped. It follows that production of 1 million barrels of shale oil a day will require the mining, processing and dumping of 2 million tons of rock, and that would require a mining operation equivalent in size to the entire United States domestic coal industry. There will undoubtedly be a large increase in coal production in the next decade, so oil shale producers will be hard pressed to find the mining capacity to support a large industry.

Another, and ultimately more intractable, problem is the shortage of water in the area, for the oil shale fields lie in a semi-arid region. Water would be required in the retorting process—although one technology under study would require very little—and since an oil shale industry will lead to large urban development, there would also be increased demand for municipal water supplies. Thus, according to an environmental impact statement published in August by the Department of the Interior, "development beyond the 1-million-barrel-per-day level is possible, but at some point water availability could place a limitation on the ultimate size (of production)". A similar conclusion is reached in a study to be published in a few weeks time by the House Committee on Science and Astronautics. Thus, mining and retorting of oil shale is likely to be limited for the foreseeable future to about 1 million barrels a day which, although significant, represents only about 5% of projected demand for petroleum in 1985.

Chiefly for these reasons, a good deal of attention is now being paid to the second technology for shale oil production, the so-called *in situ* method. If it can be perfected, *in situ* production would have the advantage that little or no rock would have to be brought to the surface and eventually disposed of, so many of the environmental problems

would not arise, and it would also use less water. The technology is not as well developed as surface processing technology, however, and according to the Department of the Interior, there are still some problems to be overcome. Nevertheless, the federal government is prepared to put more money into *in situ* research, for a five-year energy research and development plan being put together by the Atomic Energy Commission recommends that \$126 million be spent on such research by 1980.

Occidental Petroleum claims, however, to have perfected an *in situ* process which is now capable of commercial application. According to an interview with Dr Armand Hammer, the controversial chairman of Occidental, which was published in the London *Times* on November 24, the process involves blasting a chamber into the underground shale formation, injecting natural gas into it and burning the gas. Oil runs out of the shale, into the chamber, and can be pumped to the surface. Hammer made the astonishing claim that the costs of the operation are only \$1 per barrel, and he said that with massive capital investment the process could be producing large quantities of shale oil within three to five years.

Sources in the oil industry and in the Department of the Interior were sceptical of the claim last week, however, and an official of Occidental even said that he believes the claim that oil could be produced for \$1 per barrel "may have been misinterpreted". The Department of the Interior also said in its environmental impact statement that "it is obvious that considerable further improvements in *in situ* recovery are still required before industrial scale *in situ* recovery could become a reality". The impact statement also suggested that a major uncertainty in the *in situ* method is what happens to subsurface movements of liquids and gases, both before and after the retorting process. There is a possibility that toxic contaminants may find their way through the groundwaters into the Colorado River, which flows through the oil shale region and provides a lifeline for several million people who live downstream.

The Occidental process has, nevertheless, caused something of a stir among shale oil developers and *in situ* production will be closely investigated in the next few years. In fact, the two prototype tracts to be leased next year in Wyoming are particularly suitable for *in situ* production.

The vast oil shale deposits in the United States are thus likely to make a significant contribution to oil supplies sometime in the future, but they are not likely either to affect the relatively short term situation or to provide final salvation.

NUCLEAR POWER

Expected Defence

THE government's reply last week to the report of the Select Committee on Science and Technology on nuclear power chiefly defended the formation of the National Nuclear Corporation (NNC) in its current form (Cmnd 5499, HMSO, 1973).

The select committee had recommended that the government should take at least a 30% share in the new company, the remainder of the shares being open for tender. Any special management that the new company required should be provided on a contract basis, according to the select committee.

In the event, the government allowed GEC to acquire 50% of the shares and took up a mere 15% for itself through the United Kingdom Atomic Energy Authority (UKAEA).

The government says in its reply that "the basic need is for a company with the commercial, financial and managerial strength to meet the United Kingdom's requirements for nuclear power safely and to forecast cost, time of completion and performance. A company with these capabilities should also be in a position to compete successfully in the world market and would ensure that our substantial public investment in nuclear technology is exploited to the full and is suitably remunerated".

For this to be achieved, the government argues, "a unified management under the supervision of a principal shareholder who has a substantial financial commitment to the company and experience of the industry" is a main requirement.

The committee has also been worried by the prospect that GEC might withdraw from the new company. The government considers this unlikely, because GEC's financial commitment is "a serious and substantial one". Furthermore, the company has agreed not to sell its shares for five years without the consent of the government. If, later, GEC does want to sell, the UKAEA is to have first option on the shares.

The government also sets out to reassure the committee about the constitution of the Nuclear Power Advisory Board (NPAB). The committee said that unless the board was given an effective role it would be better not to appoint it. The government replies to this by stating that it sees the role of the board as being one of the greatest importance.

Equally the government defends the appointment of Lord Aldington, Chairman of the National Nuclear Corporation, to the board. The committee had argued that the construction company

should not be represented. The government says that it carefully considered the committee's comments, but believes that "NNC's views on all aspects of nuclear power development should be available to the NPAB and that this can best be achieved by Lord Aldington's membership. NNC's commercial judgment will be a very important factor in determining the direction and success of this country's future exploitation of nuclear power".

The government also declares that it is considering the committee's recommendation that the Chief Inspector of the Nuclear Installations Inspectorate should not have any other responsibilities.

The committee learned when it took evidence from Mr E. C. Williams, the Chief Inspector, that he is also the head of the Energy Technology Division within the Department of Trade and Industry. Fearing a clash of interest between the two jobs, the committee came out in favour of keeping them separate.

The government stated that it will take this into account "during further consideration of the arrangements that will be proposed for a Safety and Health Commission".

COPYRIGHT

Carry on Copying

by our Washington Correspondent

A SPECIAL appeals court in Washington DC ruled last week that the copyright laws do not prevent libraries from photocopying journal articles or pages from books. The decision, which overturns an earlier ruling by a judge of the United States Court of Claims, has been warmly applauded by scientists since it means that libraries can continue to supply them with photocopies of journal articles for research purposes. But it has been roundly condemned by publishers who claim that it will drive yet another nail into the coffin of struggling magazines.

The court also said that it is up to Congress to place limits on the amount and type of photocopying that should be allowed, so the ball is now firmly in the court of Senator John McClellan's Subcommittee on Patents, Copyrights and Trademarks, which is considering amendments to the 1909 Copyright Act (see *Nature*, 244, 535; 1973).

The ruling came in a suit filed against the National Library of Medicine and the National Institutes of Health (NIH)

AIR POLLUTION

Emission Remission

by our Washington Correspondent

ALTHOUGH motor manufacturers have so far failed in their attempts to keep exhaust catalysts off all cars sold in the United States next year, they may yet win a partial reprieve from the full force of the Clean Air Act. Last week the Senate Public Works Committee decided to recommend to Congress that the timetable for meeting the strict exhaust emission controls specified by the act be relaxed a little. The committee will recommend, in short, that the controls be applied in California next year, as planned, but that they should not be extended to the other forty-nine states until 1976. This will be a year later than planned.

If the Senate and the House of Representatives take up the committee's recommendation, it means that exhaust catalysts would have to be fitted to all cars sold in California next year, since there is not enough time to develop other technologies for meeting the standards. But they would not have to be used elsewhere in the nation until 1976.

The committee's partial retreat will not, however, please the Ford Motor Company or Chrysler, since officials from those two manufacturers argued

at public hearings early in November that Congress should not force the use of catalysts at all; instead, they contended, more time should be given for the motor companies to develop better technologies for cleaning up emissions from automobiles (see *Nature*, 246, 182; 1973).

Senator Jennings Randolph, chairman of the Public Works Committee, also announced last week that his committee is planning to hold more public hearings on a related matter—whether or not the control on emissions of oxides of nitrogen should be relaxed. The Environmental Protection Agency announced earlier this year that the original measurements of city air pollution, which led to the standards, were incorrect and that oxides of nitrogen may not be a great problem. Those hearings will be held in December or January.

It is unlikely that the Senate will adopt the committee's recommendation for relaxing the timetable specified by the Clean Air Act until it has also made a recommendation on the nitrogen oxides question. Thus, even if Ford and Chrysler manage to persuade other members of Congress that the committee's recommendations do not go far enough, it seems unlikely that Congress would be able to act in time to prevent catalysts from being installed on California cars next year.

by Williams and Wilkins Co., a publisher of some thirty-seven medical journals, including the *Journal of Immunology and Medicine*. The company alleged that the libraries had been infringing copyright laws by widespread photocopying of articles for NIH scientists and for other libraries. In 1970, for example, NIH libraries photocopied 85,744 articles (about 930,000 pages) and in 1968 the National Library of Medicine photocopied some 120,000 articles, mostly for smaller libraries which do not have subscriptions to the journals concerned.

Other publishing companies joined in the suit on Williams and Wilkins's behalf, arguing that the advent of fast copying techniques and the widespread and growing practice of passing photocopied material from one library to another is cutting into the sales of journals and will eventually force small circulation magazines out of the market. The full Court of Claims—essentially an appeals court—held last week, however, that if such photocopying is banned, medical research would suffer. But the decision was a vexed one, for the court was split four to three and one of the judges declared in a dissenting opinion that "the decision will be read that a copyright holder has no rights that a library is bound to respect". Attorneys for the publishing company have indicated that they will probably appeal to the United States Supreme Court.

In the meantime, McClellan's subcommittee is considering a bill which would allow libraries to photocopy copyright works only if they have satisfied themselves that the material cannot be obtained through the usual commercial channels. In other words, no library would be able to photocopy a scientific article for a client, without paying a royalty to the publisher, if the journal is still in print. That provision caused such a hue and cry from library organisations, however, that McClellan reopened hearings on the matter in August; his subcommittee has yet to take further action.

ENERGY

Unnatural Gas

NORTH Sea gas will not last for ever. When reserves are exhausted, which is estimated to be in about twenty years time, what will there be to replace it?

One possible candidate now being actively studied is a substitute natural gas (SNG) made from coal. A plant for producing SNG is now being tested at Westfield, Fife. This is the first time that a gas with the calorific value of natural gas, about 800 British Thermal Units (BTU) per cubic foot, has been produced from coal on a commercial

scale. The burning characteristics of the gas are also similar to those of North Sea gas and it can be used in equipment designed for North Sea gas without any expensive modification.

The Westfield plant manufactures SNG in two distinct stages. First, the well established Lurgi process is used to gasify the coal almost completely and a gas of low calorific value, or 'lean' gas, is produced. This lean gas is then enriched catalytically to give SNG. It is the catalytic enrichment (a methanation) which is the key to the production of SNG and the Gas Board is loath to reveal the full details of its operation.

The Lurgi process converts almost all the coal into gas, unlike the system used to manufacture town gas which produces coke and tar as well. The lean gas so produced provides about 176 useful therms (1 therm = 10^5 BTU) from each ton of coal used but this depends on the quality of the coal. Town gas, on the other hand, produces only 75 therms a ton even though it has a calorific value of 500 BTU compared to the 300 BTU of the lean gas. The methanation process consumes energy, of course, but 145 useful therms of SNG gas can be obtained from each ton of coal.

This demonstration plant has not, however, been built with sales in Britain in mind. It is being financed, at a cost of \$6 million, by a consortium of about twenty North American companies and is being run by a subsidiary of the Continental Oil Company in association with Scottish Gas. The Gas Board has access to the results of the project—the process design was carried out by British Gas and Continental Oil

experts—but the board regards SNG as an insurance against the future and not the solution to an immediate need. The potential importance of the project is at present centred firmly in North America.

Fourteen Lurgi plants have been built around the world but only two are still in operation: the Westfield installation and another at Cecilburg in South Africa. Successful in their day, the other plants were made obsolete when plentiful supplies of natural gas became available. The Cecilburg Lurgi, a much larger undertaking, owes its survival to strategic considerations and cheap local coal.

In the United States, the demand for natural gas is increasing rapidly and, according to some sources, the reserves will only last for another ten to twelve years. Two plants are already in operation in North America based on another catalytic process developed in Britain to obtain SNG from oil. Nine similar plants are under construction. These plants are very successful but their future is now uncertain because of the current oil shortage.

The economics of the operation at Westfield depend on the price of coal and it is hoped that by experimenting with various slagging techniques (deliberately allowing certain concentrations of slag to build up in the furnace) the cheaper, low grade coals may be used. The United States has enormous coal reserves and if the Westfield project is successful it will provide a missing link from the chain of processes necessary to convert some of these reserves into SNG. The possible application of the process in Britain is, of course, further in the future.

Short Notes

Blowing in the Wind

A NOVEL aspect of the energy crisis was revealed in *Pravda* last week (November 27). Ten million tonnes of Soviet coal are, it seems, lost annually in transit. With the increasing mechanisation of the mining industry, the proportion of the fine fraction in each coal shipment has increased and faster freight shipment means that this fine fraction is blown away from open wagons, causing a loss of up to 15 to 20% of each shipment. This costs some 5 million roubles a year in counter-pollution measures.

The Soviet Committee of National Control is considering methods to prevent this loss. The most promising would seem to be that of Professor V. Beshkov, who suggests covering the shipments with a protective synthetic film, made from waste products of the cellulose and petroleum industries. Other proposals include mechanical

compaction of the slack, coking of the coal at the pit head to eliminate transport (the losses of coke in transit are considerably lower), and such elementary precautions as sealing up cracks in the wagons to avoid coal falling on to the track.

But why not buy a few tarpaulins?

Sliding into Europe

BBC-2 is running a series of programmes under the overall title *Life in the Nine* to explain how Britain may be affected by joining the European Economic Community (EEC). The programme on November 26 dealt particularly with EEC regulations applying to road transport. In the course of it Mr Geoffrey Cave-Wood, a member of the Road Hauliers Association, said that an increase in the axle and total weights of lorries from the present British limits to the expected EEC limits would be a good thing for many reasons, one of which is that the extra weights of these vehicles would enable them to stop more effectively.

NEWS AND VIEWS

A Better Future for ISC?

FOUR years ago there was speculation in *Nature* (222, 1216; 1969) on the future of the International Seismological Centre in Edinburgh. The ISC, it was suggested, should go into the seismogram storage and distribution business and leave estimation of the principal parameters of earthquakes to the United States Coast and Geodetic Survey. The advice was not taken, which is probably just as well. The USCGS no longer exists and though its Preliminary Determination of Epicentres service has survived, the US Geological Survey, which assumed this responsibility, could well be looking for a suitable opportunity to transfer this to an internationally supported body. World Data Centre A now satisfies most needs for seismograms and WDC B is being encouraged to be more effective.

The ISC, meanwhile, has effected a welcome facelift. There seems an end to the computing difficulties which have beset the ISC since its inception. The *Bulletin* of principal data now appears monthly in a computer typeset format. The lag time of four years has been reduced to two at the behest of the governing council, thereby allowing data from even the most inhospitably sited of 800 or so reporting stations to be included. There are now twenty-four members (trustees) represented on the governing council contributing annually some £60,000 in sums of £200 upwards towards the income of the centre in Edinburgh. The deed which established the ISC in its new structure was sealed by the hosts (the University of Edinburgh) and the Royal Society. The day-to-day work of the centre is carried out by an international staff of ten under a full-time director on leave of absence from the US Geological Survey. This healthy looking organisation has come a long way in the past four years.

The primary product of the ISC is a definitive listing of the principal data of some 12,000 earthquakes per year, having magnitudes of about m_b $4\frac{1}{2}$ and greater. This is more than double the number published by the PDE service after its six-week data cut-off. The centre's amplitude and supplementary phase material, as well as its number of contributing stations (which include a well distributed sample from the Soviet Union), is superior to all others. The cost of printing of the bulletin is now the principal cause of concern. The idea of publishing it as microfiches is understandably very unpopular even at a third of its cost, yet how often, and by how many seismologists, is the full suite of bulletin data used? Not often is the probable answer and, in any case, major users almost certainly prefer the bulletin tapes.

An idea which may not have been dusted off in recent years is the use of a microfiche bulletin together with the centre's *Regional Catalogue*. The catalogue contains hypocentres, origin times and magnitudes listed by region. To many users the catalogue is the most useful publication, providing a geographical sort for selecting small

groups of earthquakes (or explosions, which are separately catalogued). Detailed information may be subsequently extracted from the bulletin. At a quarter of the bulletin printing costs, the substitution of a monthly catalogue for the bulletin makes good sense. The bulletin could be purchased *en bloc* for national centres, or separately as required by individual users. This might satisfy the majority of seismologists and all earthquake engineers.

A most useful and, it is to be hoped, growing function of the centre is the provision of special services. Custom data sorting is one example, and the UNESCO contracts for the production of the *Manual of Seismological Observatory Practice* and the seismicity map of South-East Asia are others of the way skills of a highly professional group are being exploited. The centre also provides a home (and funds if the work is likely to be beneficial to the centre's principal task) for seismologists whose research at the time requires immediate access to the world's premier collection of earthquake data.

The central reason, however, why the ISC is internationally supported is for the organised data it publishes. The only advantage of the bulletin is that it produces under one cover what is already available by searching the records of a number of centres like the PDE service and the Soviet and BCIS bulletins. Although most seismologists feel that the saving in time, as well as the greater accuracy of the additional processed data, are sufficient reasons for the existence of the centre, others want searches made for hypocentres of earthquakes not reported elsewhere, and would like to see attempts made to include data descriptive of the seismograms. It is doubtful whether the latter can ever be a substitute for personal reading of the seismogram. The attempts which the centre is already making to invite fuller reporting of phase arrivals and amplitudes may well fill all reasonable needs. The location of earthquakes from a mass of unassociated P times is a more controversial subject. Judged by the annual number of published epicentres, it is unlikely that the bulletin misses many earthquakes of magnitude m_b $4\frac{1}{2}$ or more, particularly in the Northern Hemisphere, so the principal contribution would be events up to half a magnitude below this threshold where seismological interests are narrower.

The safest criterion whereby to define a generally useful threshold might be that of unbiased world seismicity, and especially to equalise the magnitude threshold of the southern (oceanic) half of the globe with the northern. Seismologists must decide and at present only those from a fifth of the countries most concerned have any substantive influence on the scientific policies of the ISC. Curiously, some of the most seismically affected countries are unrepresented; so are international oil and construction companies which consult the centre regularly. Between them they could put the welfare of the ISC beyond doubt.

P.D.M.

T Lymphocytes in Nude Mice?

THE 'nude' mouse, homozygous for the gene *nu*, has been hailed as the ideal animal for studying the immunological consequences of athymia. Besides being topless and bottomless, it is generally considered to have, at the most, a minute and grossly abnormal thymus, and to lack thymus-processed ('T') lymphocytes. The article by Raff on page 350 of this issue of *Nature* therefore raises two important and related questions. First, are nude mice in fact totally devoid of T lymphocytes? Second, is the theta (*alias* Thy-1) alloantigen a genuine certificate of authenticity, conferred on no lymphocytes other than those which are passing through, or have graduated from, the thymic educational system?

What Raff has shown is that up to about 2% of lymph node and spleen cells from nude mice fluoresce when exposed to specific fluorescein-conjugated anti-theta antibodies. This proportion is very low in comparison with normal mice and implies that nudes possess perhaps 3% or less of the usual complement of theta-positive lymphocytes. The number of mice examined is small, but they come from three different sources, and comparable observations have been made in another laboratory (Lameline *et al.*, *J. exp. Med.*, **136**, 984; 1972).

The origin of the theta-bearing cells is still a matter for conjecture. The *nu/nu* thymus may perhaps show some transitory function in foetal life, allowing a few T lymphocytes to sneak through. Certainly, as shown recently by Pritchard and Micklem (*Clin. exp. Immunol.*, **14**, 597; 1973), nude mice possess progenitor cells which differentiate to thymocytes and functioning T lymphocytes in the environment of a grafted thymus. The possibility that T lymphocytes cross the placenta from the phenotypically normal (*nu/+*) mother is now open to test, since in germ-free or pathogen-free conditions *nu/nu* females can (contrary to previous belief) produce young. It is still not clear how much of the thymic educational process demands residential attendance within the thymus and how much can be achieved by postal tuition (thymic hormones or activation factors). Such factors would presumably cross the placenta more readily than cells.

This leads on to the second question. To rephrase it: is the theta antigen marker any use? As Raff makes clear, the antigen is not confined to thymocytes and T lymphocytes, but is present on epidermal cells, a component or components of the nervous system, and probably elsewhere. Apparently nude mice carry theta in these locations (Komuro and Boyse, *J. exp. Med.*, **138**, 479; 1973), and it is very unlikely that its appearance there depends on any thymic influence. By contrast, it is stated to be absent on lymphocytes of non-thymic lineage, and it is on this belief that its value as a marker depends. Boyse and his colleagues (most recently in *J. exp. Med.*, **138**, 1027; 1973) have found that theta may be induced to appear on the surface of previously negative cells (including *nu/nu* spleen cells) by a variety of *in vitro* tricks. These include brief exposure to thymus extracts of several origins, but also to other substances (bacterial endotoxin, polyadenylic-uridylic acid and cyclic AMP) whose relevance to the thymus is more debatable. So far, few functional tests on these induced cells have been reported. The modification of sensitivity to azathioprine in rosette-forming lymphocytes exposed to thymic factors

(Bach and Dardenne, *Immunology*, **25**, 343; 1973) may be a related phenomenon, but again the functional significance of the change is obscure. There is therefore no compelling reason at present to conclude that nude mice harbour any functional T lymphocytes.

Against the immunofluorescence data must be set experimental results from several laboratories, almost all of which suggest that thymus-dependent functions are absent. But it takes a refined experiment indeed to distinguish between profound depression and total ablation. For many purposes the distinction is probably not very important, but in situations where it may be critical one should, in the words of the old Scottish motto, 'gang warily'.

H. S. M.

Probing Lunar Carbon

CARBON compounds of biological significance have not been detected in lunar samples. Elucidation of the unusual chemistry of the element carbon in the non-biological lunar environment, however, continues to provide a fascinating challenge. Two of the analytical approaches which have been used to study the part per million concentrations of carbon present are pyrolysis and acid dissolution: pyrolysis gives a measure of total carbon without distinguishing its chemical state; acid dissolution measures the concentrations of gaseous hydrocarbons (CH_4 , for example) and carbide but gives no measure of total carbon. Both methods have shown that most of the carbon in lunar soil has derived from sources outside the Moon, principally implantation by the solar wind and, to a lesser extent, by impacting meteorites. Indeed, the amounts of carbon and its compounds give an indication of the degree of exposure of the constituent soil particles at the Moon's surface. The particles are carried through a cycling process of erosion and aggregation, mainly brought about by micro-meteorite bombardment. Large grains are eroded to smaller particles which are, in turn, aggregated into more complex grains, such as glass welded agglutinates. Carbon added from extralunar sources is originally accumulated at particle surfaces but, during aggregation, a proportion of the carbon species in the smaller particles is incorporated into the newly formed composite particles to give a volume-related carbon component.

In a recent issue of *Nature Physical Science* (**246**, 65; 1973), Desmarais *et al.* suggest that this volume-related component, measured by extrapolation of plots of total carbon against the reciprocal of particle radius, is a better indicator than total carbon of the time of exposure of a soil sample at the surface of the Moon. They believe that the rate of recycling by erosion and aggregation is faster than the rate of accumulation of carbon from outside the Moon and conclude that the carbon species found on the Moon are not directly relatable to source because of "blurring" caused by the rapid recycling process.

The outlook for the further unravelling of lunar carbon chemistry may not be as bleak as this hypothesis suggests, although the complete history of the constituent carbon atoms will probably never be known. Other lunar in-

investigators believe that more detailed sample analysis, including single particles, and simulation studies of ion implantation and meteorite impact will throw light on the respective roles of the solar wind and meteorites in bringing about the synthesis of the observed carbon compounds. Thus, in a recent contribution to *Nature Physical Science* (245, 3; 1973) Pillingier *et al.* suggest that the chemically detected iron carbide present may have derived by dissolution of carbon in submicroscopic droplets of metallic iron; these Ångström sized droplets seem to have been formed from ferrous iron and solar wind implanted hydrogen during the flash heating induced by micrometeorite impacts.

The unusual synthetic reactions which occur during the evolution of lunar soil particles should therefore continue to provide a fascinating challenge in surface chemistry for some time yet. Just how to solve a number of crucial questions remains to be seen. For example—what is the chemical state of the major proportion of the carbon?

From a Correspondent

TROPONIN

A Molecular Latch?

from a Correspondent

MUSCLE contraction is known to involve the sliding of thick filaments past thin filaments. The control of the contraction by Ca^{2+} ions is thought, at least for vertebrate skeletal muscle, to involve changes in the structure of the thin filaments. Each thin filament is an assembly of three proteins—actin, tropomyosin and troponin—and the way in which these proteins interact and are controlled by Ca^{2+} is currently attracting considerable attention.

In the thin filament, long rod-like tropomyosin molecules are thought to be joined end-to-end to follow the two long-pitched strands of the actin structure, each tropomyosin molecule being associated with seven actin subunits. One molecule of the Ca^{2+} -sensitising protein troponin is attached to each tropomyosin molecule. Changes in the X-ray diffraction pattern of muscle on contraction have suggested that the binding of Ca^{2+} ions to troponin causes the string of tropomyosin molecules to move with respect to the actin structure from a position relatively far from the groove between the two actin strands to a position near the groove. One current hypothesis is that sites on the actin subunits are thereby uncovered and can then interact with the cross-bridges of the thick filament. Conversely, the

removal of Ca^{2+} ions from troponin causes the opposite movement of tropomyosin so that the actin sites are no longer available and relaxation is possible.

In order to understand how this movement of tropomyosin can occur, the interactions which troponin makes with actin and tropomyosin need to be defined. The problem is further complicated by the fact that the troponin molecule contains three kinds of subunit—troponin-T (molecular weight 44,000 in chicken), troponin-I (mol. wt 23,000) and troponin-C (the calcium-binding subunit with a molecular weight of 19,000). All three subunits are required for relaxation in actin-myosin-tropomyosin systems. Which of these troponin components binds to actin and which to tropomyosin?

For some time, it has been appreciated that the troponin-T subunit can bind to tropomyosin (which is why the subunit is so named). Hitchcock, Huxley and Szent-Györgyi (*J. molec. Biol.*, 80, 825; 1973) now produce new evidence that even when troponin-T is excluded, a complex of the other two subunits, troponin-I plus troponin-C, can bind quite strongly to actin-tropomyosin provided that Ca^{2+} ions are absent; in the presence of Ca^{2+} ions the binding is poor. Tropomyosin itself, however, cannot bind the complex of troponin-I and troponin-C; this is deduced from the fact that the appearance of tropomyosin paracrystals or the viscosity of tropomyosin in solution is not altered in the presence of these components. Since troponin-C by itself has no affinity for either tropomyosin or actin, the troponin-I subunit must be responsible for the binding to actin. This result fits in well with observations by other groups (notably that of Perry) that troponin-I can inhibit actomyosin ATPase in the absence of tropomyosin.

Hitchcock *et al.* propose as a working hypothesis that each troponin molecule is bound to the thin filament at two sites: one involves a strong Ca^{2+} -independent interaction between the troponin-T subunit and tropomyosin; the other involves a Ca^{2+} -dependent interaction between the troponin-I subunit and actin. Both interactions are required to obtain relaxation. Calcium, by binding to troponin-C, in some way reduces the binding of troponin-I to actin but has no effect on the binding of troponin-T to tropomyosin.

It has always been difficult to imagine how if troponin bound only to tropomyosin it could cause relative movements of actin and tropomyosin on binding Ca^{2+} ions. Now that there is evidence that troponin can also bind to actin in the absence of Ca^{2+} ions, it is possible to speculate how this movement might be brought about. For example, in the absence of Ca^{2+} , the

tropomyosin might serve to secure the tropomyosin molecules to the actin structure in the position producing relaxation, whereas in the presence of Ca^{2+} the troponin would no longer bind to actin and the tropomyosin molecules would be free to adopt the position producing contraction. At all events, with five polypeptide components and at least five types of protein-protein contact the thin filament clearly provides an abundance of interactions for the allosterically-minded.

JUVENILE HORMONE

Delayed Effects

from our Insect Physiology Correspondent
ONE of the most promising effects of the juvenile hormone and its synthetic mimics, considered as potential agents for pest control, has been the disruptive action they can exert on subsequent development when applied to the pregnant female or to the developing eggs. In some insects not only can embryonic development be so upset that the eggs fail to hatch, but apparently normal larvae may show signs of excessive juvenile hormone production in the later stages of development: they may give rise to non-viable 'adultoids', or intermediates between larva and adult, at the time when they would have been expected to undergo normal metamorphosis.

This delayed effect was at first attributed to the persistence of traces of the active substance as a contaminant of the egg shells from which the treated insects had emerged. But Riddiford and Truman (*Nature*, 237, 458; 1972) proved convincingly that in the linden bug *Pyrhocoris apterus* there is a lasting disturbance in the secretory activity of the corpus allatum in the treated insects. It seems that in such insects the corpus allatum continues to secrete juvenile hormone in the fifth instar and thus to maintain larval characters when the insect should have become adult. Excision of the corpus allatum from such larvae led to normal metamorphosis; transplantation of their corpus allatum into normal fifth instar larvae caused these to transfer into adultoids.

Effects of this sort do not occur in all insects. In the cabbage butterfly *Pieris* there is no such delayed effect on metamorphosis. It has now been shown by Hunt and Shappirio (*J. Insect Physiol.*, 19, 2129; 1973) that in the lesser milkweed bug *Lygaeus kalmii* the excessive hormone secretion, induced by the application of juvenile hormone analogues to the developing embryo at about the time of blastokinesis, will not only prevent proper metamorphosis of the fifth instar but will lead to the distinctive colour pattern of the early larval instars being retained in the later

instars—a result which supports the view that the morphological changes during development, even before metamorphosis, are controlled by the level of juvenile hormone secretion.

The long delayed effects of hormone treatments during the perinatal period are a matter of concern for clinicians (*Science, N.Y.*, **181**, 189; 1973) because it has been found in vertebrates that steroids and other hormones administered at the time of birth can induce malignant tumours, as well as changes in behaviour, in adult life.

CANCER RESEARCH

Tokyo Meeting

from a Correspondent

THE 4th International Symposium of the Princess Takamatsu Cancer Research Fund, which opened in Tokyo on November 6, discussed differentiation and control of malignancy.

G. Tompkins (University of California, San Francisco) began the meeting by reporting that nuclear sites can distinguish between two cytoplasmic steroid receptors, which bind to DNA or chromatin, but not to RNA. S. Ohno (City of Hope Medical Center, California) demonstrated the simplicity of mammalian regulatory systems with an elegant example from the (*Tfm*) androgen-receptor protein locus on the X chromosome of the mouse. The mammalian embryo, he suggests, has an inherent tendency to develop as a female; male development must be induced by an androgen. Therefore, he says that the X-linked *Tfm* locus is the one and only regulatory locus which determines sexual phenotypes of mammals.

J. Paul (Beatson Institute, Glasgow) described experiments confirming the thesis of a positive regulatory role for non-histone chromosomal proteins. Non-histone proteins from erythroid cells allow brain chromatin to transcribe globin genes. The mechanism of control of transcription was discussed in the light of Paul's recently published model for the structure of chromatin. This proposes that the transcriptional unit in eukaryotes is similar to that in prokaryotes and that non-histone proteins bind to or near promoters to permit the attachment of RNA polymerase which cannot otherwise enter the DNA-histone supercoil.

The new nuclear polymer, poly (ADP-ribose), was introduced by S. Shall (University of Sussex). He described the general properties of this polymer which is made by a chromosomal enzyme; NAD^+ is the substrate, DNA and histone stimulate the activity of the synthetic enzyme, cyclic AMP inhibits the enzyme which hydrolyses the polymer and the polymer seems to be covalently attached to chromosomal

proteins. The specific activity of the synthetic enzyme fluctuates markedly in lymphoid cells during the transition from the non-growing to the growing state. Also, it varies during both the cell generation and the growth cycle. There is some evidence that it is involved in the regulation of DNA replication. The physiological function of this chromosomal enzyme system is unknown at present. Shall suggested that these enzymes of nuclear NAD metabolism directly integrate NAD and cellular energy metabolism with DNA biosynthesis both in progression through a single cell generation and in modulation of growth rate. In particular, he suggested that poly (ADP-ribose) may function by regulating the initiation of succeeding sets of replicons.

An explanation for the Pasteur and Crabtree effects was proposed by S. Weinhouse (Fels Research Institute, Philadelphia) who suggested that competition between pyruvate kinase and mitochondrial respiration for available ADP could account for these two phenomena.

A very simple and ingenious technique for the detection of abnormal differentiation of the gastric mucosa has been developed by T. Sugimura and colleagues (National Cancer Centre, Tokyo). It uses diagnostic Test-tapes to detect disaccharides in gastric mucosa. Investigations with cyclic AMP and the differentiation of neuroblastoma cells in culture suggested to K. N. Prasad (University of Denver) that a chemotherapeutic regime worth investigation would be a combination of sodium butyrate, dopamine and a cyclic AMP phosphodiesterase inhibitor.

Induction of functions by 5-bromodeoxyuridine (BUdR) is being increasingly useful. H. Koyama and T. Ono (Cancer Institute, Tokyo) described the induction of alkaline phosphatase for which DNA synthesis is required. Melanoma cells become contact-inhibited and unpigmented in BUdR (S. Silaghi, Cornell University, NY). DNA synthesis and cell division seem to be obligatory. Tumorigenicity is also partially or completely suppressed.

Studies with cell hybrids are very informative, but the general tenor of the reports at this meeting called for caution and prudence in interpreting data and in drawing general conclusions about the nature of malignancy and its suppression.

M. Hozumi and colleagues (National Cancer Centre, Tokyo) are studying a protein factor which induces differentiation with a loss of tumorigenicity in cultured leukaemia cells.

The meeting ended with a thought-provoking discussion of the general nature of cellular differentiation and its relationship to malignancy which was sparked off by H. Holtzer (University of

Pennsylvania). This was a welcome addition to the attention to particulars with which most scientific meetings rightly concern themselves.

This meeting was stimulating and very informative. Its success is due tribute to the excellence of Japanese science and to the wisdom of Imperial patronage of science and especially of cancer biology, biochemistry and molecular biology.

PESTICIDES

Pests on File

from a Correspondent

THE use of computers in pesticide research was considered at a joint meeting of the Pesticides Group and Physicochemical and Biophysical Panel, Society of Chemical Industry, on October 15.

Aspects of modelling the behaviour of pesticides and pests were first considered. The panel chairman, I. J. Graham-Bryce (Rothamsted Experimental Station), stressed in his introduction that models are greatly simplified compared with the real situation and assumptions must be selected carefully and, ideally, confirmed. The sensitivity of the model to various factors can then be explored and thus critical ones can be identified. R. C. Bridges (Plant Protection Ltd, Jealott's Hill Research Station) considered penetration of a pesticide applied to the surface of a wheat leaf and its subsequent movement through the xylem. Several pathways into the leaf are feasible and the equations for the multi-compartmental model can be solved on a digital computer. The permeability of the pesticide in the leaf is critical: too rapid penetration can lead to accumulation and possible phytotoxicity; too efficient transport through the xylem may concentrate the compound in the distal parts of the lamina and provide insufficient protection to the remainder.

J. M. Osgerby (Shell Research Ltd, Woodstock Laboratory) considered applications of the analogue computer, which can simulate physical systems, to the addition of the molluscicide trifenmorph to water in an irrigation canal complex in Egypt (*Pestic. Sci.*, **1**, 5; 1970). Trifenmorph was added at one point upstream of the area to be treated. The main feeder canal carried water continuously to storage dams from which small canals ran to fields that were irrigated for 10 h daily from Monday to Friday, inclusive. By varying factors such as dosage, the time and duration of the trifenmorph, the optimum conditions were deduced within the limits of the model. Osgerby also considered examples of the diffusion and leaching of pesticides in soils treated with various formulations (*Pestic. Sci.*, **3**, 753; 1972).

Following work at the Glasshouse Crops Research Institute, the predatory mite, *Phytoseiulus persimilis*, is widely used in the United Kingdom to control the glasshouse red spider mite, *Tetranychus urticae*. H. G. Fransz (Netherlands Institute for Marine Research, Texel) discussed three ways of simulating the predation of *T. urticae* eggs by *Typhlodromus occidentalis*, which is used in Holland, considering factors such as prey density and predator gut content. His stochastic approach, in which the system changes state according to a series of random numbers, was run 100 times for each prey density to determine the mean values and 95% confidence limits. In his deterministic simulation random events were replaced by continuous rates of change and a hypothetical mean run once for each prey density and so forth. In his compound method gut content was divided into five states and a deterministic model applied to each (and to other factors split into states). For given conditions he found differences in the number of eggs attacked between stochastic and deterministic models with the compound method nearer the second model.

The use of computers in information storage and retrieval was then considered with R. A. E. Galley in the chair. J. A. Silk (Plant Protection Ltd, Jealott's Hill) discussed the value of computers in technical information services, in providing information summaries on which management decisions can be based and explained how relevant references to published literature are provided from commercially available tapes. Clearly for an organisation the size of Imperial Chemical Industries computerised sorting and retrieval of information are essential, a point reinforced by G. Palmer (ICI, Pharmaceutical Division), who stated that more than 135,000 compounds are stored in the company's file with details of their biological activity, availability and Hansch parameters. He explained how their structures are stored in the Wiswesser Line Notation (WLN), letters and numbers standing for specific chemical groups. When the memory is searched for compounds of the required type on an atom for atom basis the rate is only 350 compounds per minute, so a preliminary sorting is needed to reject most unwanted compounds, for example a one fragment search runs at 50,000 and a WLN search at 4,000 compounds per minute.

D. T. Sagers (Fisons Ltd, Agrochemical Division) explained that testing compounds for biological activity enabled those with desirable properties and the relationship between activity and chemical structure to be identified and he illustrated this by structures (again in WLN) with specified pesticidal

activity and recalled by computer. J. C. Wickham (Wellcome Foundation, Berkhamsted) showed how computers can be used to undertake probit analysis, to determine the relative potencies of a series of related compounds and to predict the properties of aerosol mixtures, containing, for example, an insecticide, a synergist and a knock-down agent. Costs of the components can be included in the program and the commercially optimum recipe can be decided.

H. S. Stammers (Shell Research Ltd), introducing the discussion, asked whether too much of computer time is spent on statistical analyses, the results of which are of questionable value, and warned that the study of model systems can become expensive. Several of the audience agreed with earlier speakers that the next stage is a greater use of on-line computers which can be interrogated directly.

IRON-SULPHUR PROTEINS

Low Redox Potentials

from our Photosynthesis Correspondent
CAN membrane bound iron-sulphur proteins with midpoint redox potentials lower than -530 mV be involved in the primary photochemical events of chloroplast photosynthesis? This is a question posed from recent work of Ke, Hansen and Beinert (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 2941; 1973). It is about 3 years since Malkin and Bearden

(*ibid.*, **68**, 16; 1971) first suggested from electron paramagnetic resonance (EPR) studies that a membrane bound ferredoxin may serve as a primary low potential electron acceptor for photosystem 1 (S1). Since then work from several laboratories has supported the idea that an iron-sulphur centre accepts electron from the light activated S1 reaction centre (P700). Several lines of investigations have indicated that the redox level of the reduced iron-sulphur centre was lower than -250 mV and could possibly be -470 mV.

By carrying out redox titrations with digitonin-fractionated S1 subchloroplast particles monitored by low temperature (13 K) EPR spectroscopy, Ke and his colleagues have uncovered some new and striking properties of membrane bound iron-sulphur proteins. They have resolved three different iron-sulphur centres: one with resonance lines at $g=2.05$ and 1.94 ; one with lines at $g=2.05$, 1.92 and 1.89 ; and one detected by a single line at $g=1.86$. Redox titrations between -450 and -610 mV carried out at pH 10 indicated that the midpoint potentials of these iron-sulphur species fall into two distinct separate regions, -530 ± 5 mV and 580 mV. The redox reactions of each of the membrane bound iron-sulphur centres were found to be reversible and apparently involved a two electron change. Although all three centres could be reduced by light at room temperature, at 77 K illumination did not bring about photoreduction beyond that

Magnetic Fields in Neutron Stars and White Dwarfs

IN a supernova explosion the interior of a star may be imploded to form a neutron star or white dwarf and, as the electrical conductivity of stellar material is high, magnetic flux should be conserved during the implosion. As a result an initial field of only 100 gauss can be converted to 10^{12} gauss in the resulting neutron star. If pulsar neutron stars are typical, neutron stars do have magnetic fields of strength about 10^{12} gauss. In addition a small minority of white dwarfs have strong fields of order 10^7 gauss. Although flux conservation during implosion may account for the neutron star fields; it is perhaps surprising that most pulsar neutron stars seem to have magnetic fields of about the same strength, for stellar fields before implosion may have very different strengths.

Present theories of supernovae produced by explosive carbon burning suggest that a remnant white dwarf or neutron star can only be left if the onset of the explosion is delayed by the occurrence of convection in the interior of the star. Without cooling by convection the explosion is catastrophic

and no remnant remains. In *Nature Physical Science* next Monday (December 10), Ruderman and Sutherland suggest that this convection produces the magnetic field which is amplified in the final stages of implosion. They suggest that convection will amplify any initial field until its energy is in equipartition with the energy of the convective motions. Using estimates of convective velocities based on the mixing length theory of convection, they predict a field of 10^{12} gauss in neutron stars and one of order 10^7 gauss in what they take to be a small minority of white dwarfs formed in supernova explosions.

This is a very promising suggestion although some of its details are controversial; for example, the mixing length theory may not give a very good estimate of convective velocities. It has never been proved convincingly that an equipartition field must be produced by the interaction of magnetic fields and convection and the field produced by such interaction might be a small scale field rather than a large scale field of strength 10^{12} gauss. These points will no doubt be discussed in future

accomplished electrochemically, at about -560 mV.

These observations are particularly striking since it would place the iron-sulphur species detected by Ke *et al.* at the strongest reducing level known for a biological electron carrier. So far it is difficult to assess the involvement of all these species in primary S1 activity especially because of the temperature sensitivity of the iron-sulphur centres with midpoint potentials beyond -560 mV. Bearing this in mind the results indicate that the chemical potential, generated between the primary donor (P700) and primary acceptor, of S1 due to the absorption of photon energy, could be at least 0.96 or possibly 1.01 eV.

SPACE RESEARCH

Observing Satellites

from a Correspondent

A DISCUSSION meeting on satellite observations and their use in orbital analysis was held at the Royal Society on November 17. The meeting, organised by the Optical Tracking Subcommittee of the British National Committee on Space Research, was designed to bring together the volunteer visual observers of artificial satellites, whose observations (some 25,000 per year) are so valuable in determining satellite orbits for subsequent analysis in geophysical research.

The meeting began, appropriately enough, with a talk on the visual appearance of satellites by D. M. Brierley (Royal Radar Establishment, Malvern), who emphasised that non-spherical satellites can suffer great variations in brightness when the solar phase angle is unfavourable. J. A. Pilkington (Scarborough Planetarium) discussed some of the difficulties in finding reliable information for listings of newly-launched satellites, and some old ones too. Recent geophysical advances resulting from analysis of orbits were described by D. G. King-Hele (Royal Aircraft Establishment, Farnborough): he mentioned the new determination of the Earth's pear-shaped polar section (*Nature*, **246**, 86; 1973), and discussed the evaluation of fifteenth-order harmonics in the geopotential from analysis of orbits at fifteenth-order resonance; good values have now been obtained for harmonics of order 15 and degree 15, 17, 19...27. Next G. E. Perry (Kettering Grammar School), accompanied by a tape recorder, regaled the audience with a medley of interesting radio signals from recent satellites caught during his untiring pursuit of transmissions from satellites.

The observers attending the meeting had previously answered a comprehen-

sive questionnaire running to seventy-eight questions, prepared by M. D. Waterman (Elliott Automation, Frimley), who reported some interesting features of the statistics. As might be expected with observations relative to the stars, the results of the survey showed that observational accuracy improves with experience: observers are at their best after more than 10 years' practice. An astonishing contrast to this finding was provided by sightings of the flaming decay of satellites: the regular observers at the meeting had made more than a quarter of a million observations and had scanned the night sky for thousands of hours, yet only one of them had seen a decay; but the minority of the audience who were not regular observers included four defiers of the laws of chance, who had seen a decay. There were further contributions from A. J. G. Moorat (Appleton Laboratory, Slough), on satellite predictions; from G. E. Taylor (Royal Greenwich Observatory), on time standards; from R. D. Eberst (Royal Observatory, Edinburgh), on recent work at Edinburgh; and from J. Hewitt (Ordnance Survey), who gave a very clear description of the techniques for laser tracking of satellites.

EARTHQUAKE PREDICTION

No Dilatancy

from our Geomagnetism Correspondent

BECAUSE of bad communications, early Russian work on the changes of seismic velocity associated with earthquakes took a long time to become known in the west, and even more surprisingly in Japan. Thus although as long ago as 1962 Kondratenko and Nersisov (*Trudy Inst. Fiz. Zemli*, **25**, 130; 1962) had reported that the velocity of P waves in the crust increases after moderately large earthquakes in the Tadzhikistan region of southern central Asia, this secret apparently remained locked inside the Soviet Union until Savarensky (*Tectonophysics*, **6**, 17; 1968) reviewed the results in English. Moreover, even then the Russian studies were treated with some scepticism. Rikitake (*Earth-Sci. Rev.*, **4**, 245; 1968), for example, argued that the 30% change in elasticity implied by a reported 15% change in P wave velocity threw doubt on the validity of the original data.

Nevertheless, the appearance of Savarensky's report, other reports of Russian work, and particularly an article by Semenov (*Izv. Acad. Sci. USSR Phys. Solid Earth*, **4**, 245; 1969) giving details of premonitory seismic velocity changes, inspired United States seismologists to search for similar effects. Semenov had shown that before earthquakes in the magnitude range 3-5, the

velocity ratio v_p/v_s decreased by about 6% and then increased back to its normal value just before the main shock. A few years later, Aggarwal *et al.* (*Nature*, **241**, 101; 1973) reported similar results involving decreases in v_p/v_s of up to 13% for New York earthquakes in the magnitude range 1-3. But the really important result was obtained recently by Whitcomb *et al.* (*Science*, N.Y., **180**, 632; 1973), who showed that 4 years before the 1971 San Fernando earthquake of magnitude 6.4 the v_p/v_s ratio decreased suddenly by 10% from its average value of 1.75 and then gradually rose back to about the average value at the time of the main event. Equally importantly, Whitcomb and his colleagues were able to propose a plausible physical mechanism for these changes in terms of rock dilatancy.

Whitcomb *et al.* also found that the greatest contribution to the change in v_p/v_s occurred in v_p and thus argued that, because man-made explosions produce mainly P waves, the path to earthquake prediction could be opened up by the use of artificial sources "such as large mine blasts" rather than being limited to the vagaries of earthquakes. This challenge was taken up by McEvilly and Johnson (*Science*, N.Y., **182**, 581; 1973), who have examined the travel times of P waves from Californian quarry explosions of well known origin times. The results are disappointing to say the least. To put it bluntly, McEvilly and Johnson find no velocity changes associated with earthquakes at all.

The quarry at which the sixty-eight examined explosions occurred between July 12, 1961, and June 14, 1963, lies near Salinas, California. The P waves from the blasts were recorded at the University of California's seismic stations, some of which have been in operation continuously since the early 1960s and the nearest of which lies about 13 km from the quarry (equivalent to a P_g wave travel time of 2.5 s). The uncertainties in reading the P wave arrival times were estimated to be less than 0.1 s, although there were, of course, other possible sources of variation in travel times. For example, some of the blasts were not timed at the quarry, and their origin times had to be inferred to within 0.1 s on the basis of arrival times at the nearest station. But McEvilly and Johnson estimate that the maximum error possible, including that arising from a 10% dilatancy-induced velocity change over the distance to the nearest station, would give arrival times at a particular station within a range of ± 0.4 s about a mean value. Thus for mean travel times of 8.6-28.0 s to the seven stations used (excluding the nearest station), the extreme variations would be $\pm 5\%$ at the nearer stations and $\pm 1.5\%$ at the more distant stations.

In fact, the travel times and velocities to all seven stations were all within $\pm 2.0\%$ of their respective mean values, and most were within $\pm 1.0\%$. Moreover, the measurements with the largest deviations from the means are most easily accounted for by known sources of error such as source locations and origin times. And, finally, a comparison with the times of occurrence of earthquakes in the magnitude range 4.5–5.5 gave no indication whatsoever of any premonitory velocity changes prior to the earthquakes.

McEvilly and Johnson suggest four possible explanations of these results. The first is that although the dilatancy effect exists, it was not observed in this case because of poor sampling in time. But this argument is held to be weak because, notwithstanding the sampling problem, at least one change of greater than 2% would have been expected, especially bearing in mind the occurrence in the area of a large number of earthquakes with magnitudes less than 4.5. The second explanation also assumes that the dilatancy effect exists but that it is obscured by poor sampling in space. This requires that the effect of a velocity decrease of at least 10% in the earthquake source region should be such as to give an overall velocity change of less than 2% out to the recording stations; and this in turn requires that the region affected by dilatancy in the vicinity of magnitude 4.5–5.5 earthquakes should be less than 10–20 km in diameter. Such restrictions, however, do not seem to be impossible.

The third possibility is that the region investigated is uniformly dilated as a result of either the usual seismicity in central California or of an impending major earthquake. The main argument against such a situation is that the v_p/v_s ratio seems to be "normal" at about 1.75. The final explanation proposed is simply that dilatancy is not an important effect at all in the vicinity of a major strike-slip fault, possibly because either the stress levels are insufficient to cause dilatancy or, if sufficient, are more or less stable without large fluctuations.

So where does that leave the general question of premonitory seismic velocity variations? The answer is probably that there has been little real change. These new results must certainly temper the euphoria induced by the Whitcomb report; but at the same time they emphasise that the data are insufficient to support either of the extremes of pessimism or optimism. Assuming that one snowflake makes a winter is no more justified than seeing the summer in a single swallow. The fact is that although the McEvilly–Johnson results are consistent with the absence of the dilatancy effect, there seems to be at least one explanation which does not

preclude dilatancy. On balance the evidence is still somewhat in favour of the existence of premonitory seismic velocity changes.

MATERIALS

Fatigue in Composites

from a Correspondent

THE subject matter of the twelve contributions presented at a symposium on fatigue in composites organised by the Institute of Physics at Imperial College, London, on November 15, ranged widely. The fields covered included the behaviour of metal matrix composites reinforced with metal fibres and with whiskers; fatigue resistance of a variety of carbon fibre and glass fibre reinforced plastics, laminates and joints under different forms of loading; the setting up of safe-life design criteria for the use of composites in realistic conditions; and non-destructive testing

techniques for studying damage sustained during testing and in service. Both in prepared papers and in discussion it was clear that three principal topics claimed the attention of the participants, both investigators and users: not surprisingly, these three are fundamentally interrelated.

The first topic concerns the question of variability of fibre and composite properties, and defects in manufactured materials. J. Sturgeon (Royal Aircraft Establishment, Farnborough) discussed the importance of using failure probability analysis in order to obtain usable stress/life curves for fatigue of carbon fibre reinforced plastics (CFRP). From discussion following his remarks and also those of A. K. Green (Imperial College, London), it became clear that it is not generally possible to extrapolate results from one batch of material to another, or from one laboratory to another. This fact considerably impedes the procedures of developing and using

Sinistral Movement Along the Great Glen Fault

WHAT movement has taken place along the Great Glen fault? This is a question which has received a variety of answers, most of which conflict with each other. When Kennedy (*Quart. J. Geol. Soc.*, 102, 41; 1946) first recognised the fault as transcurrent, for example, he assumed that the Caledonian Strontian and Foyers granitic complexes had once been part of the same intrusion and concluded from this that a sinistral displacement of 100 km had occurred. A year later he found further support for the same conclusion from the matching of the metamorphic zonation in the Moinian assemblage rocks. But during the past few years, not only have differences in the Strontian and Foyers intrusions been found, thus throwing doubt on the identity between the two, but the grades of metamorphism in the Moinian rocks surrounding the two intrusions have also been found to differ.

Going to the other extreme, Holgate (*Scott. J. Geol.*, 5, 97; 1969) has adduced evidence for a Mesozoic dextral displacement of 30 km along the Great Glen fault, and Garson and Plant (*Nature*, 240, 31; 1972) have even more recently claimed that the Caledonian movement was dextral. Clearly someone is wrong somewhere; but one of the difficulties in identifying who it is, or who they are, is that data are so often so incomplete that they may be taken to support directly opposing views simultaneously. Nor has geophysical evidence been of much direct help apparently. On the other hand, geophysical data have had something to say about which other faults are, or are not, continuations of the Great Glen fault.

Leannan fault in Ireland whose well-established sinistral displacement of 40 km circumstantially supports a sinistral movement along its Scottish counterpart.

This is part of the background against which J. A. Winchester, in *Nature Physical Science* next Monday (December 10), adduces evidence to support a sinistral displacement of 160 km along the Great Glen fault. What Winchester has done is to investigate the variations in metamorphic grade in the Moinian assemblage on each side of the fault and thus produce a metamorphic zonal map—a feat made possible by the widespread distribution of calc-silicate gneisses in the assemblage. In other words, he has been able to map the regional variations of metamorphic grade on each side of the fault in terms of the mineralogical variations in the calc-silicate gneiss bands and the distribution of gneissose injections. The characteristics of the zonal map are too complicated to be summarised here; but what can be said in general terms is that the variations in metamorphic grade, and in particular the maxima and minima, can be adequately matched across the Great Glen fault only if a sinistral movement of 160 km is assumed to have taken place. The features of the match are numerous; but the most dominant example is that the high grade rocks of the Western Highlands complex and the Monadhliaths injection complex, both of which are truncated diagonally by the fault and both of which have about the same width at the fault line, are brought into juxtaposition when the pre-displacement

design criteria for fatigue in composites. The question hinges, as M. J. Owen (University of Nottingham) pointed out, on one's inability to define exactly the nature of defects in reinforced plastics and their likely effect on static and cyclic properties. N. J. Parratt (Explosives Research and Development Establishment, Waltham Abbey) observed that although in whisker reinforced aluminium alloys the minute whiskers do not *per se* act as flaws or crack starters, unfortunately it happens that the effects of small defects in such materials are larger than could be expected from fracture mechanics investigations on larger, more easily studied defects.

The second topic concerns the appropriateness or otherwise of the experimental work that is currently being carried out. Owen took up the point made by a member of the audience, that uniaxial fatigue tests on simple aligned or biaxially-oriented composites were hardly likely to provide information that would be useful for realistic design problems. He showed how a fracture mechanics approach could be used to develop safe-life design criteria for notched plates of glass reinforced plastics. A. W. Cardrick (RAE, Farnborough) gave added weight to these arguments when, during his paper on the properties of CFRP/aluminium composite joints, he listed as being most urgently required information on the effects of secondary stresses and stress concentrations, accidental damage, joint design and cumulative damage characteristics. He also emphasised that constant amplitude and frequency loading conditions were not as useful as narrow band random loading.

The third important question—fatigue damage—was also discussed by W. S. Carswell (National Engineering Laboratory, East Kilbride), who described an approach to defining residual strength of fatigued composites in terms of a damage function which, however, is extremely difficult to define, is even more difficult to measure and is likely to be different in different types of composite. Of particular importance in this respect were the contributions of W. N. Reynolds (Atomic Energy Research Establishment, Harwell), who discussed non-destructive testing methods as a means of assessing fatigue damage, and those of C. Kim (Chelsea College, London) and of M. Fuwa (University of Sussex), who showed how acoustic emission detection techniques can be used to give information about the damage sustained during loading and cycling of test pieces or components. It could well be that these non-destructive testing methods will have to be used in conjunction with design criteria in order to overcome or allow for the deleterious effects of variability and manufacturing defects.

NUCLEAR THEORY

Heavy Ion Transfer

from our Nuclear Theory Correspondent

MANY studies of nucleon transfer reactions between heavy ions have shown typically bell-shaped angular distributions centred at angles around 30° . These distributions can easily be understood using a classical model of the interaction. The lighter of the two ions approaches the heavier along a Coulomb hyperbolic orbit and the reaction in which a nucleon is transferred from one ion to the other is most likely when this orbit just grazes the surface of the heavier ion. For larger impact parameters the lighter ion passes beyond the nuclear field of the heavier ion and no nuclear reaction can take place. For smaller impact parameters the ions interact strongly and many complicated reactions take place, so that the probability of the simple transfer reaction is again reduced. Thus there is a maximum in the cross section at the angle corresponding to the deflection characteristic of a grazing collision, and it falls for smaller and for larger angles giving the observed bell-shaped curve.

Quantum mechanical analyses of such reactions can be made using the distorted wave theory and taking into account finite range and recoil effects. These are generally in agreement with the data but in some cases they have shown rapid oscillations superposed on the overall bell-shaped curve. It thus becomes interesting to see if these rapid oscillations can be detected experimentally and also if they can be understood theoretically. This has recently been done by a group at Brookhaven National Laboratory (Chasman, Kahana and Schneider, *Phys. rev. Lett.*, **31**, 1074; 1973).

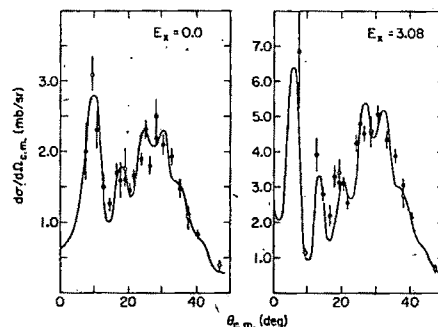
They measured the differential cross section for the proton-transfer reaction $^{48}\text{Ca}(^{14}\text{N}, ^{13}\text{C})^{49}\text{Sc}$ to the ground and 3.08 MeV states of ^{49}Sc at an incident energy of the nitrogen ions of 50 MeV. Preliminary data (open circles in the figure) showed the expected bell-shaped curve at 30° but with an additional peak at about 10° . The first distorted wave calculations gave a smooth bell-shaped curve without the forward peak but it was found that if the absorbing part of the optical potential describing the motion of the incident particle is slightly reduced, the forward peak appears and in addition oscillations of higher angular frequency (about 6°) appear on the bell-shaped curve.

Further measurements were therefore made to see if these oscillations are real, and the solid points on the figure show that this is indeed the case. The distorted wave calculations reproduce these complicated oscillations remarkably

ably accurately, confirming the reliability of the calculations.

The physical origin of these small-angle oscillations is still not understood. Diffraction theory suggests that they must be associated with a distance of the order of the diameter of the target nucleus, so the obvious explanation is that they are due to interference between the projectile paths on opposite sides of the target nucleus. This is confirmed by calculations starting with the quantum mechanical expression for the cross section and using approximate analytical forms for the partial wave amplitudes and phases. It is then possible to obtain an expression very similar to those of classical diffraction models consisting of two terms, corresponding to interactions on opposite sides of the nucleus. The form of the cross section is then determined by the relative magnitudes of these terms, which varies with the incident energy and the interaction potential.

At low energies the classical scattering angle corresponding to grazing collisions is large, the two terms do not interfere and the classical bell-shaped cross section results. At higher energies the scattering angle is less, and the small-angle oscillations appear superimposed on the classical cross section. The onset of these oscillations depends on the absorbing potential. The lower this potential the lower the energy for which the incident particle feels the real nuclear potential and so the lower the energy at which the oscillations appear.



Differential cross sections for the proton transfer reaction $^{48}\text{Ca}(^{14}\text{N}, ^{13}\text{C})^{49}\text{Sc}$ to the ground and 3.08 MeV states of ^{49}Sc at an incident nitrogen energy of 50 MeV, compared with distorted wave calculations which include recoil.

The distorted wave calculations also allow the absolute magnitude of the transfer cross section to be related to the spectroscopic factor for the single-particle transition. The values extracted from the experimental results are found to be in excellent agreement with the nuclear structure calculations of Cohen and Kurath.

This work shows nuclear transfer between heavy ions is very well understood theoretically, so that it is now a powerful method of obtaining information on nuclear structure.

The Individual and the Information Problem

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This article deals with the needs and habits of scientific authors and readers.

THERE is little doubt that the cost of providing scientific information is increasing. In the six years ending in 1972 the mean cost of medical journals¹ has increased by 64% and that of general scientific and technical journals by 48% both increases being greater than that of general retail prices² which increased by 38%. The total purchases by scientific libraries have increased even more, for more journals are now being bought. Analysis of the costs of eight science libraries which in 1972 spent £38,000 on journal and book purchases shows they are well over double what they were six years ago.

Those who request librarians to purchase information are members of the community who produce the information. The whole system is thus a closed one, a matter which those concerned with commercial aspects of journal production have not been slow to realise. The system has been much studied by information scientists, indeed a new discipline 'bibliometrics' has emerged as a result³, and most of this work has confirmed and extended de Solla Price's earlier analysis of science as a totality^{4,5} to show that growth of information is exponential and parallels the increase in size of the scientific community. An alternative approach is to study the habits and assess the views of the individuals who contribute to the totality; this at least begins to define the operational needs of scientists. In addition such an approach enables an exploration to be made of the relation between the individual and the whole scientific community, for publication of the individual's work is the main link in this relationship. Whether growth of the mass of publications, the fragmentation of disciplines, the emergence of new sub-disciplines, and the fact that most scientists are paid employees, affect the concept of a universality in science are equally relevant questions.

Aberdeen Studies

For these reasons we have made a series of studies within three biological research institutes in Aberdeen, each of which publishes a report which describes its work. These, the Rowett Research Institute, the Macaulay Institute for Soil Research and the Marine Laboratory, deal with a series of disciplines relating to marine, soil, plant and animal studies. The workers have but a small educational commitment: their views and habits may well differ from those of

university lecturing staff, and for this reason they are called 'working scientists'. No logical inferences should be drawn from this terminology. The three institutes together publish 150 primary scientific papers (excluding reviews and popular articles) per annum, and the mean number of authors per paper ranges from 1.7 for the Marine Laboratory to 2.2 for the Rowett Institute. The three libraries in total subscribe to 1,862 primary journals and 121 abstract or other secondary journals, and each has a full-time library staff. Questionnaires of various sorts elicited replies from about 150 people, which represents about an 80% return of those approached.

It can be argued that the sample was small relative to the total number of biological scientists in Britain, or that it was in some way unrepresentative, so that the results lack generality. The concordance of results from the three institutes does not suggest this to be so. They nevertheless suffer from the defects of most surveys of opinion; what an individual believes, what he is willing to say he believes, and what may be inferred about his beliefs from analysis of his actions, differ. This has to be kept in mind in analyses which reflect motivation. The results are summarised in three parts, first those relating to the habits and views of workers as authors of primary papers, second their habits as readers and seekers of information, and third in terms of their underlying beliefs about the role of communication in science in the 1970s.

Working Biologists as Authors

An analysis of *curricula vitarum* of those workers who had published more than ten full papers showed that $76 \pm 14\%$ (s.d.) of their papers were published in three journals and that this was true even of the most prolific who had published more than 100. The remaining 24% were spread over many journals, each adding on average 0.6 of a journal to an author's list. This skewness of the distribution of journals and papers for individual workers is equally true of whole institutes. Figure 1 shows the total output of primary papers for each institute in six years against the number of journals in which these were published. It shows that most papers are published in a small proportion of the total journals used. Most surprising is that in all three institutes, catering for such a wide range of biological subjects, their 883 papers were published in only 168 journals. Furthermore, 76% of them could be accommodated in but thirty-four journals. Half the journals only occurred in the list because they had accepted one paper in the six-year period. These 'peripheral' journals were either very highly specialised ones, or journals competing with older established ones in a growing field and, from the dates of their first issues, were on average the younger journals.

This factual account of publishing habits at the three institutes can be equated with the views of individuals. Workers were asked to how many journals they could submit their current researches when complete. The results are shown in Fig. 2. They show the median number to be six. What these biologists chose and the reasons for choice are summarised in Table 1. Outstanding was the concern of the worker with the reputation of the journal within his field of study. Status is gained by publishing in such journals. The circulation of the journal—a matter relating to the universality of science—and delay in publication were not important considerations. Workers were not much interested in the format of journals though they were prepared to express forthright preferences for particular formats, methods of expressing and preparing references to previous work, standardisation of nomenclature and other editorial practices.

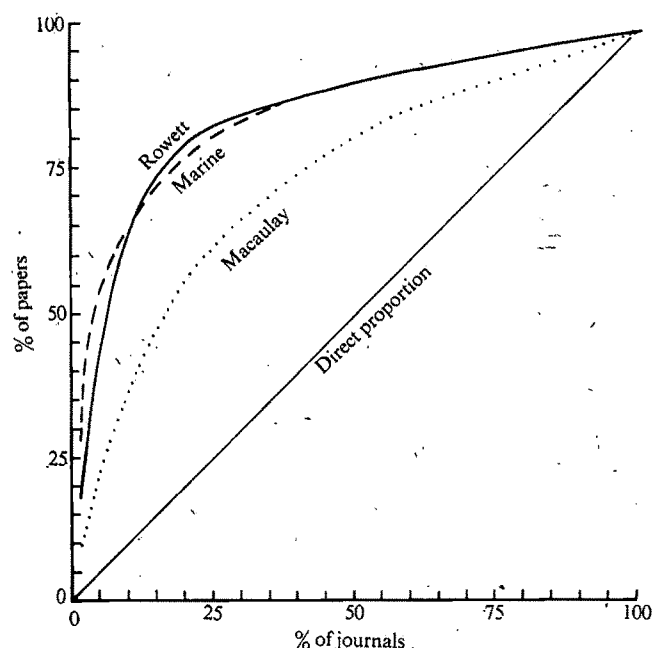


Fig. 1 Cumulative percentage frequency curves based on six years' publication of work by three institutes. The Rowett Institute published 423 primary papers in eighty-three journals, the Marine Laboratory 301 papers in fifty-seven journals and the Macaulay Institute 154 papers in fifty-two journals.

The wide choice of journal which workers state they have, and the very limited range of journals in which they in fact publish during their working lives, prompted us to ask whether they thought there were too many journals in their fields of interest. Most workers (63%) were not prepared to comment but of those who did 78% thought there were too many. Asked whether as a corollary there was not a case for amalgamation of journals, possibly on an international basis, more opinions were expressed; 34% were against and 25% in favour. The reasons given for rejection of the corollary were first that standards of journals might be threatened by amalgamation, and second that some work was of national rather than international scientific interest.

It would thus seem that individual biologists have a small number of journals in which they prefer to publish and to which they adhere during their working lives. They aspire to publish in journals with high reputations, and are not primarily concerned with the widest possible audience for their work, possibly thinking—and this was not examined—that secondary journals will bring their work to the notice of the whole community.

Table 1 Factors Stated to be Considered in Making a Choice of Journal in which to Publish Work by Workers in Three Research Organisations in Aberdeen

	Rowett Institute	Macaulay Institute	Marine Laboratory	All
The reputation and standards of the journal	85	85	84	85
The presence of papers on the same subject	78	85	90	83
The circulation of the journal	63	47	42	53
The delay between receipt of manuscript and its publication	34	43	35	38
The format of the journal	6	19	13	12
Number of respondents	68	47	31	146

Figures show percentage of total respondents who thought the factor important.

Working Biologists as Readers

The use of published material is of two types, first a fairly immediate one to identify new advances, and second a retrospective one undertaken to identify what has been accomplished in a particular field. The former is best called current awareness and the latter information retrieval.

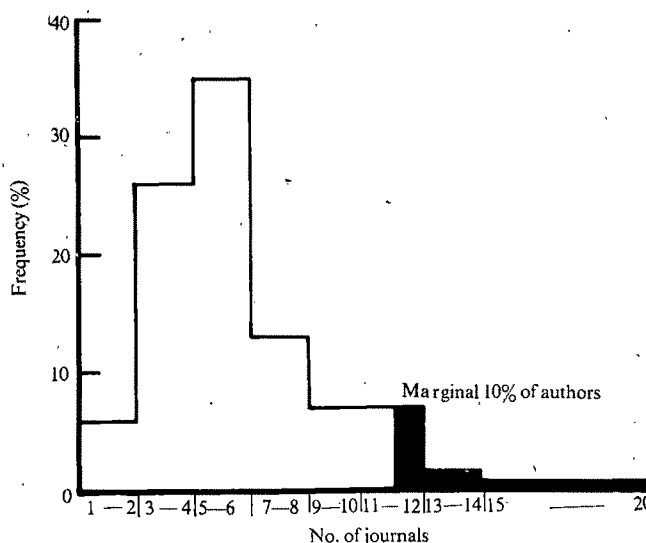


Fig. 2 Number of journals to which workers stated that the results of their current research work could be submitted. The data refer to all institutes and the median is six.

Using a variety of approaches it was quite clear that these biologists had no difficulty in keeping aware of current advances in their particular fields of research interest. Ninety-four per cent stated that they could keep up with current advances in their own fields and 39% even thought they could keep up with work within their own disciplines. Such a question in some ways predicated the answer, for to admit that one could not keep abreast of one's own speciality would imply an incompetence. Less open to interpretational difficulty were the answers to the question "How many primary journals should you read to give a 90% coverage of your field of research interest?". These are summarised in Fig. 3 from which it is evident that the median was twelve

and that 90% of all respondents would gain 90% satisfaction if each was given funds to buy twenty-five journals.

The methods used by workers to keep aware of current work varied slightly, but not significantly, from institute to institute. Half the awareness came from a scanning of primary journals as they arrived in their libraries and a quarter from a scanning of review or abstract publications, a practice which accepts delay in the acquisition of information. The remaining quarter was accounted for by a scanning of lists of paper titles such as *Current Contents* or through colleagues drawing attention to particular papers.

Having, through a scanning process or in other ways, identified a paper relevant to his work, a worker usually wishes to ensure that he can find it again. The methods used to preserve current information were examined to show that 15% relied on their memory, 54% made a reference card or slip and 31% preserved the whole paper either by requesting a reprint of it or by making a photocopy. Photocopying was three times more important than requesting a reprint, indeed a variety of evidence suggests that reprint exchange as a method of scientific intercourse is in decline. Asked how far they relied on discussion and correspondence for dissemination of information, only 19% acknowledged that this method of communication was important. (See also Table 4 where a similar estimate of importance emerges from a different survey.)

It would thus seem that the individual's immediate needs for information are met by a small number of primary journals, a very small number indeed when judged by the hundreds scanned by abstracting journals. In addition, the scanning process is used to generate a highly personal retrieval system by most workers.

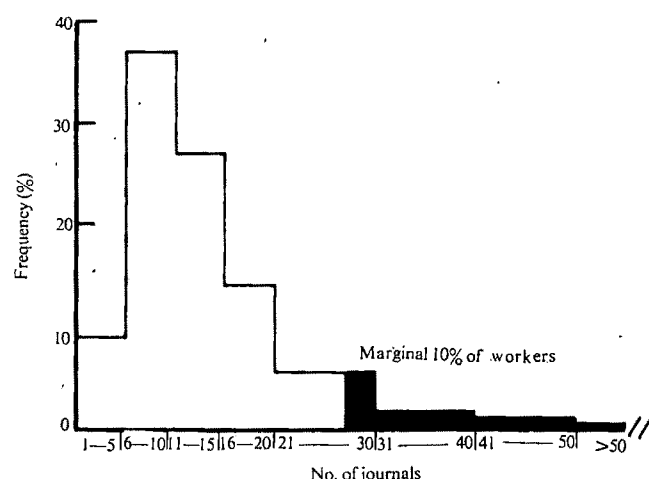


Fig. 3 Number of journals which workers stated that they should read to provide a 90% coverage of their field of research interest. All institutes, median is twelve.

Figure 4 shows the number of times workers stated they searched for information in the previous month. The median number was four times and 90% of workers searched less than ten times per month. Problems encountered in tracing what was published were not great for the Rowett and Macaulay Institutes but at the Marine Laboratory 42% of respondents acknowledged they had difficulty. It was evident that the major entry point in a literature search was not a perusal of the indexes of abstract journals or the use of computerised retrieval systems. Rather it was the references listed at the ends of primary papers or review articles. The entry points for the three institutes are shown in Fig. 5. Usage of abstract journals was checked at one institute. Consultations were less than 0.3 times per month per worker.

The workers were asked to recall on how many occasions they had referred to pre-war and nineteenth century literature.

Their replies suggested a very considerable reference to this older literature; 31% stated that they referred to nineteenth century literature. Analysis of library borrowings and inter-library loans, however, did not suggest that this older literature was consulted in depth, for only 4% of all borrowings and 11% of all inter-library loans were for material published

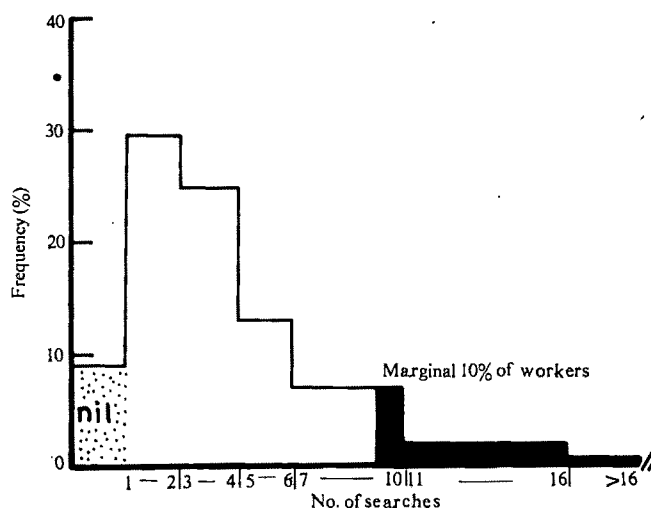


Fig. 4 Number of times workers stated they had searched for information in the previous month. All institutes, median is four.

before 1950. This anomaly is curious. Perhaps the question was equivocal; the term 'referred' could have been interpreted as 'considered' rather than 'perused', and the recollections do not necessarily imply that the paper or work was read in the original.

Library Policies

It has been implied that librarians are under pressure to purchase journals, and, being librarians, they like to preserve what they have purchased in a systematic way. They can never provide 100% satisfaction for all their readers from their own resources, and without inferring that they respond to pressures in any arbitrary way it can be suggested that their purchasing policy could be rationalised on the basis of the above analysis of opinion and habit. The argument is as follows.

If 76% of an individual's work is published in three journals irrespective of his prolificacy and if 76% of an institute's work over a contemporary period is published in fifteen, and if the shapes of the marginal distributions are similar, then that institute covers five 'fields'. Fields so defined are in terms of journals and the definition is not independent of the interpretation by journal editors of what constitutes their subject matter. Then, if 90% of the workers obtain 90% coverage of their current research interest from twenty-five journals, the number of journals to be taken by an institute with five fields is $5 \times 25 = 125$. This number should give 90% satisfaction to 90% of its users and a library so defined is a working library. It should have a working life and it can be argued from the pattern of borrowings and loans that this should be 25 years, for direct reference to work published a quarter of a century earlier is less than 5% of total reference. The precise cut-off obviously depends on the cost of shelf space relative to the cost of book postage, it being assumed that a network of archival libraries exists and that efficient and legally trouble-free methods of photocopying are in operation.

The libraries of the three institutes differed. Two, those of the Rowett Institute and Marine Laboratory, cater for

more than the immediate needs of their staffs and are regarded as major libraries in the sense that they are United Kingdom repositories for information in nutritional sciences and marine sciences respectively. The library of the Macaulay Institute does not have such a wide additional commitment. The Rowett library and Marine library are seven and eleven times the size they should, in theory, be were they working libraries. The Macaulay library of 290 primary journals, however, is not much greater than the size inferred from these theoretical

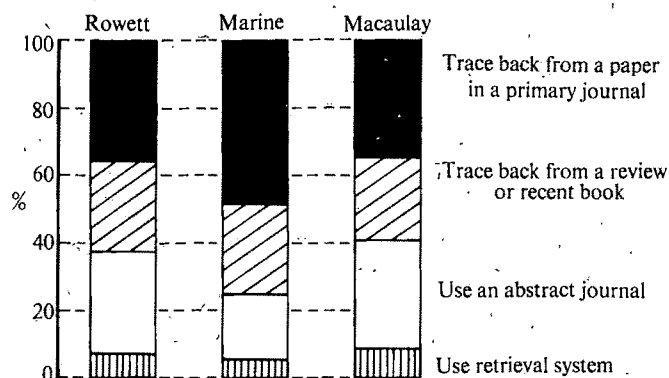


Fig. 5 The methods stated to be used to trace work already done in a particular field by workers in three institutes.

considerations—200 journals. There was no evidence that the workers at the Macaulay Institute had any greater problems in keeping aware of current work or in information retrieval than did workers at institutes housing the two larger libraries. This suggests that the arguments about optimal size of library are correct.

Beliefs about Scientific Communication

Communication of research findings through publication in a journal with a referee system is central to the whole social system of science. It is the way in which the individual relates to others in the scientific community. Traditionally and ideally it is held that the individual scientist makes his work known through publication and receives in return approbation and esteem among his fellows. The exchange is free and the judgment is by equals bound by no contractual relationship. The exchange is not simply here and now but international and through time; it is also basically disinterested and the participants non-competitive. Merton⁶ has stated "The substantive findings of science . . . constitute a common heritage in which the equity of an individual is severely limited."

This traditional ideal—if it ever existed in an unalloyed state—is subject to erosion and change, because of the growth of science, its increasing complexity and its institutionalisation. The intrinsic control processes in which communication is the main feature are more and more in conflict with external ones. Scientists are also employees, while government and industry finance research with particular ends in view. Furthermore, the media of the exchange process—the primary scientific journals—are under commercial pressures and a growing proportion are under commercial control.

It has frequently been suggested^{7,8} that these problems, combined with the pressures caused by growth and fragmentation of science as a whole, are destroying the basic value system on which the scientific activity is based; in other words that the 'breakdown' of the publication system, if indeed a breakdown exists, not only illustrates the practical problems of 'big science', but also involves a fundamental change in the motivations and belief systems of

scientific workers. It therefore seemed of interest to try to find out to what values the workers at these three institutes were willing to subscribe. Did they still uphold absolutely the 'ideal' values, despite the practical problems? Did they, at the other extreme, take a defeatist view and suggest that these values no longer had any relevance? Or did they find some compromise, easy or uneasy?

The workers were asked questions designed to represent this spectrum. They were offered a list of statements and asked which represented their view most nearly; if necessary they could (as a form of compromise) choose more than one. Questions were designed to explore beliefs about the system of publication. Briefly, they ask first: is the ideal of a universality of knowledge practicable?; second: is the 'reward' system in fact operating equitably?; and third: is the scientist's responsibility to participate in the system still rigorous, despite the problems of scale?

Table 2 Classification of Replies to the Question: When you Write a Paper, for what Potential Audience do you Feel that you are Writing?

	Percentage of respondents		All
	Age 39 or below	Age 40 or above	
The whole scientific community	14	9	12
The members of one discipline (for example, chemists, physiologists)	42	51	46
The members of one sub-discipline (for example, lipid chemists, rumen microbiologists)	35	32	34
A small number of interested people most of whom you could name	9	6	8
No audience—writing papers is only a ritual activity	3	5	4
Number of respondents	88	65	153

It has been suggested⁵ that the traditional methods of communication and control can be maintained only if new groupings, new subdisciplines, provide an audience of practicable size. The workers were therefore asked whether they still held the ideal value that work is addressed to the whole scientific community, or whether they saw themselves as focusing on smaller groups. Their replies are given in Table 2 where they are classified by age; in the surveys of opinion which follow differences between institutes were minor. It was perhaps a little surprising that, despite the trend towards the narrowing of specialties, nearly half of these workers claimed to be writing for the members of a whole discipline, and a substantial proportion thought that they were addressing 'the whole scientific community'. The younger workers, perhaps because they were less distant from the socialising processes of scientific education, were rather more inclined to envisage the traditionally wide audience. In general, these answers would seem to suggest a conflict between the traditional values of scientific publication and the practicalities of the current situation.

A second question concerned the efficient and impartial working of the reward system. The replies are given in Table 3. Again, these answers might be thought to show some conflict, and some doubt in these workers' minds about the impartiality of the system and the traditional value of individuality. Few thought that 'rewards' were influenced by organisational status, but a third thought that the reputation of the laboratory was a factor, and only about a fifth, overall, thought that credit was given wholly impartially.

Evidence of disillusion came also from answers to a

question designed to assess the apportionment of credit for work reported in a multi-author paper. Two-thirds said that they used their personal knowledge while names on papers were thought by 7% of the workers to have a decreasing relevance nowadays. This perhaps suggests a concern about the operation of the traditional system of reward.

Table 3 Replies to the Question: Which of the Following would you say is Most True at Present?

	Percentage of respondents		All
	Age 39 or below	Age 40 or above	
Scientific work is invariably judged on its merits, irrespective of who the author is	20	25	22
Reaction to work is influenced by the reputation of the laboratory or organisation in which it is done	39	31	36
Reaction to work is influenced by the author's scientific reputation	54	55	54
Reaction to work is influenced by the author's status in his organisation	7	4	6
A young and unknown worker would have difficulty in getting unconventional work accepted, unless well sponsored	22	19	21
Number of respondents	87	68	155

The purpose of a third question was to find out what these workers thought of the scientist's obligation. Did they wish to uphold the rigorous traditional view that their first duty was to share their work? Or, in the face of the current difficulties, did they see their obligation as merely to 'keep up' in a general or a specialised way?

Table 4 Replies to the Question: Which of the Following best describes the Obligation of the Scientist with regard to Communication?

	Percentage of respondents		All
	Age 39 or below	Age 40 or above	
He has an obligation to see that others in his field know what he is doing	34	26	32
He has an obligation to see that he knows what is being done in his field	75	59	66
He ought to keep up with the key journals in his subject	30	37	33
He ought to maintain personal contact with others working in his field	18	12	16
It is impossible to keep up with the literature nowadays	7	4	5
Number of respondents	87	68	155

Few people were willing to say—even anonymously—that they thought the system of communication had broken down completely. Their views of their obligations were on the whole rigorous, whether or not it was practicable for them to fulfil them. The younger scientists were more

to have a rather more idealistic view of the possibility of 'keeping up' in their field.

Implications

Though on a small scale, though confined to biologists with no educational commitment and though, like many investigations designed to ascertain belief, plagued by uncertainty, the investigations provide evidence that the scientific community can cope with a so-called information explosion which apparently causes consternation to librarians, archivists and information scientists. Individuals use very few journals; they actually publish in a small number and they do not contemplate doing otherwise; they identify a number of key journals to read which is a minute fraction of the many thousands which could be regarded as relevant to their fields of research. The individual thus copes by narrowing the overall information problem to a practical size. Even on the scale of whole research institutes there is evidence that the information problem is not immense, for large groupings can be inferred to take place.

These behavioural patterns imply that some of the classical ideals of science no longer apply and that the universality, communality and disinterestedness of science have been tempered by practical expediency. Yet many workers still subscribe fully to these ideals and are reluctant to admit that times have changed. In correspondence some castigated practices of multiple publication, the splitting of work into separate parts and the publication of short papers rather than complete accounts of work, adducing reasons why quantity of publication appeared to them to be more important than quality as far as individual advancement in a career sense was concerned. Certainly, besides the conflicts between practical possibility in information transfer and the ideals of the universality of knowledge there are additional conflicts implicit in publication which relate to the professional and scientific status of a worker and the financial reward which he receives. The old saw 'publish or perish' has financial overtones as well as those of approbation.

It has to be recognised that there are limits to the capacity of individuals to assimilate information and that each individual research worker studies within a limited range. It also has to be recognised that journals are articles of commerce subject to laws of supply and more particularly of demand. It can be envisaged that journals will continue to proliferate and divide to cater for these limited demands of workers but that new economic difficulties will emerge as a result. Equally proliferation raises a series of problems about the achievement of high standards in terms of acceptance policies within such journals, for not only is the quality of a journal important to the individual who publishes therein, but it also relates to the whole value system of science which quite clearly individuals are unwilling to jettison. These problems are some of the more pressing ones that the scientific community has to face at the present time.

We thank those who responded to our various questionnaires and who corresponded with us. Mrs A. MacDonald helped in the collation of the results.

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Search for Short Bursts of Gravitational Radiation

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Recent data from an experiment in Glasgow suggest that pulses of gravitational radiation of less than a few milliseconds duration are too infrequent to account for signals reported by Weber in 1970.

WEBER's experiments^{1,2} have for some years suggested the presence of unexpectedly large bursts of gravitational radiation coming from outside our Solar System. The bursts last less than 0.5 s, and one or more is detected per day. Here we report the development and operation of detectors designed to give much more precise and detailed information than could be obtained with the original Weber detectors and on observations with these instruments.

Our detectors consist basically of two separate masses linked by piezoelectric transducers to monitor changes in separation, an arrangement equivalent in some ways to the Weber bar but giving much larger coupling between the mechanical and electrical systems. This results in a relatively large electrical output, so that it becomes practicable to use amplifiers of wide bandwidth and to record the motion of the masses with a resolution of the order of a millisecond. (A similar arrangement was originally proposed by P. Aplin, University of Bristol.) If one considers an idealised detector with point masses and a weightless transducer, the apparent force acting on each mass can be deduced from the strain in the transducer. In fact a simple analogue circuit can be used to derive the effective force induced by a gravitational wave from the electrical output of the transducer. This filter circuit has a null at the resonant frequency of the mechanical system, since the resonance corresponds to motion without external forces. With a filter which has a response which is the inverse of that of the mechanical system the whole arrangement becomes effectively non-resonant.

Gravitational radiation detectors of this general type have been analysed theoretically from different points of view by Gibbons and Hawking³ and Buckingham and Faulkner⁴, who have shown that for a short pulse input, the output signal-to-noise ratio is proportional to $(\beta Q)^2$, where β is the coupling constant between the mechanical and electrical systems, and Q is the quality factor of the mechanical resonance. This signal-to-noise ratio is not the only factor to be considered in assessing the sensitivity of the detector in an actual experiment, but it is an important one, and large values for this factor have been achieved in our detectors. The wide bandwidth, good time resolution, and high sensitivity of these detectors give one the possibility of detecting short bursts of gravitational radiation signals in

a much more detailed and critical way than is possible with other currently available detectors.

Detector Arrangement

A schematic diagram of one of our detectors is shown in Fig. 1. The two aluminium half-bars are bonded to six stacks of piezoelectric transducers, and each half-bar is suspended at its centre of gravity from an aluminium support structure which is itself supported at its centre by a bridge. This bridge is a flat aluminium plate resting on stacks of lead blocks separated by pieces of rubber which provide the main isolation from vibrations. The whole detector assembly sits on a trolley which rolls into the vacuum tank on rails. Each detector has a mass of 300 kg and a total length of 155 cm.

The signal from the transducers passes to a field-effect transistor amplifier and then through the filters F1 and F2. The filter F1 is a bandpass filter used to define the bandwidth of the system; the band transmitted is approximately from 650 Hz to 1,450 Hz, centred near the fundamental frequency of the detector. The filter F2 is used to extract the signal from the resonant motion of the detector. In some of our experiments an analogue computer circuit which solved the equation of motion of an idealised detector was used; its frequency response is shown in Fig. 2a. With this filter the complete system reproduces the main features of the input force waveform, but the rapid increase in gain at high frequencies does increase the noise level of the system. If the waveform information is of less importance than the signal-to-noise ratio, a filter with a narrower notch is useful. The simple LCR filter shown in Fig. 3, with the response of Fig. 2b, is convenient. With this filter, the measured performance of our system for bipolar pulses was close to that predicted for the optimised filtering system of Buckingham and Faulkner⁴.

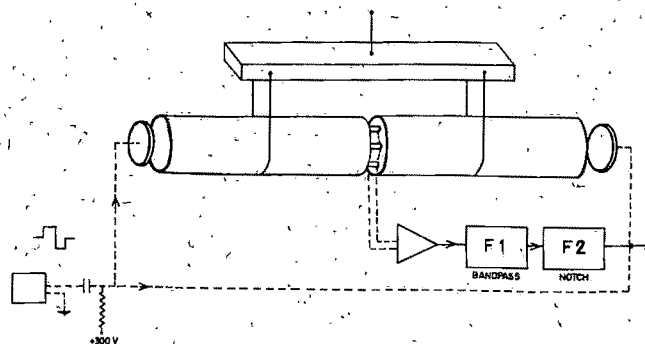


Fig. 1 Schematic diagram of one of the detectors, including the arrangements used for applying calibration forces to the bars.

Calibration and Sensitivity

The system was calibrated by applying forces of known magnitude and waveform to the ends of the detector by the electrostatic attraction of a pair of fixed electrodes. The signals were superimposed on a fixed polarising voltage, as shown in Fig. 1. The steady force applied to the detector in this arrangement is ignored by the electronic system, and the effective force change is closely proportional to the alternating test voltage waveform. Calibration was done with bipolar pulses of total duration equal to the detector period. For one of our detectors, $\beta=0.18$, $Q=2,200$, the resonant frequency is about 1,100 Hz and the mean output noise corresponds to about $0.015kT$. The other detector, the first which we built, had slightly poorer performance with $\beta=0.05$, $Q=1,400$, resonant frequency of about 1,020 Hz and a mean output noise corresponding to $0.033kT$.

The sensitivity of our experiment may be expressed in terms of energy thresholds, which we define operationally as follows. In the case of a single detector test force pulses are applied, and the amplitude of the pulses is adjusted so that the output of the notch filter triggers a threshold discriminator for 50% of the pulses. Then the energy which such a pulse would feed into the first longitudinal mode of a detector which was initially at rest—that is a bar system with no thermal excitation—is calculated and expressed in terms of the thermal energy kT of a normal mode of the real detector. This energy we define as the '50% threshold' of the single detector. This idea may be extended to a two-detector coincidence experiment, where it is convenient to define a '25% threshold' at which coincident test pulses of equal equivalent energy are detected by the coincidence system with an efficiency of 25%. It may be noted that if the two detectors are not of equal sensitivity this threshold will not correspond to the 50% efficiency point of each detector individually.

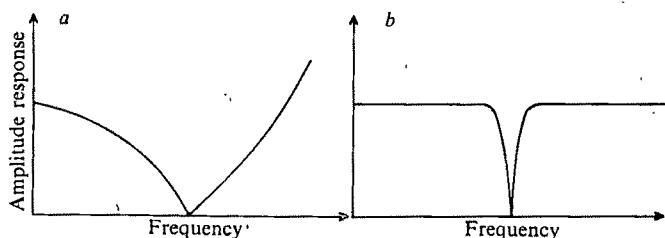


Fig. 2 Frequency response of an inverse filter for an idealised detector (a) and of a simple LCR filter (b).

In our present experiments the thresholds varied somewhat among the different recording techniques used. For one detector the 50% threshold lay in the range from 0.12 to $0.15kT$ for the main recording systems. The corresponding 50% threshold for the other detector varied between 0.2 and $0.5kT$ during the period of the experiments.

The experiments described here are most sensitive for short pulses of duration 3 ms or less, which might be expected from gravitational collapse, and so are not such sensitive tests for longer pulses which might be detected by Weber's equipment.

Preliminary Experiments

It was suggested some years ago by Weber¹, and more recently by Bertotti (private communication), that the forces caused by gravitational waves in the bar of a detector might release stored energy, so that a magnified signal might be obtained. We have therefore carried out experiments to try

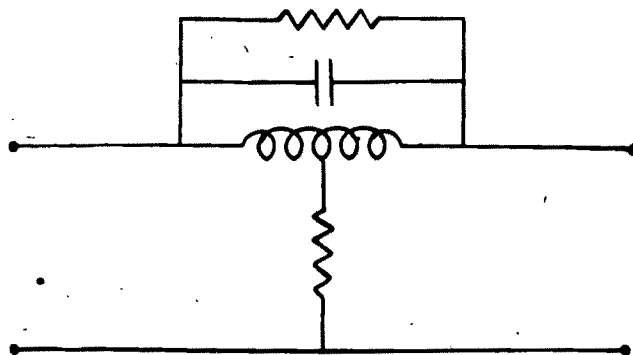


Fig. 3 LCR notch filter used to extract changes in the amplitude and phase of the resonant motion of the detector.

to observe such a process. In one test we applied impulsive forces to one of our detectors, of an amplitude just below our detection level, and at a rate of 8.64 d^{-1} . The time of occurrence of each was indicated by a subsequent train of large pulses which were easily seen. In a run lasting about two months, none of the small pulses became detectable. Another test was made using a train of five equal amplitude force pulses (corresponding to a mean energy change of several times kT) separated by intervals of 20 s. The train of pulses was repeated 8.64 times per day. One might have expected any amplification process to be more effective for the first pulse of a train than for the last, if the recovery of stored energy in the bar is a slow process and the first pulses in a train have depleted the accessible energy. We in fact see no significant change in observed pulse height. From these results and also from the agreement of our calibration measurements with calculated predictions, we conclude that there is no important multiplication process in this detector. More details of this and other experiments with a single detector have been presented elsewhere^{5,6}. (Some of the results presented now differ slightly from those given in ref. 6, as a result of more extensive and precise evaluation of the data, and incorporation of additional observations.)

Coincidence Experiments

For these observations the two detectors were set up 50 m apart, with their axes north-south. (The latitude is 56° N.)

A simplified schematic diagram of the arrangement used for data recording throughout the present experiment is shown in Fig. 4. The chart recorder and the time delay analyser use only the notch filter output. The coincidence system is triggered from the notch filter output, but other signals, some of them seen before the notch filter, are recorded on the photographs.

The chart recorder monitors the notch filter output from the two detectors as well as other signals for test purposes. As our wideband detectors can give output signals of duration a few milliseconds or less a pulse-stretching technique is used with the chart recorder to ensure that the pens do not miss any pulses.

For highest sensitivity, a recording device faster than the chart recorders must be used. We have therefore developed a system for photographic recording of data displayed on an oscilloscope, triggered by electronic coincidence circuits. The signals from one detector are delayed by 0.8 s in an f.m. tape recorder and the same threshold discriminators and coincidence circuits look concurrently for both prompt and delayed coincidences between the two detectors. The photographs of prompt and delayed coincidences look similar, and are marked in a way which is not apparent to the person scanning the records until after the photograph has

been measured, thus minimising the effect of human bias in the analysis. The signals pass through digital delay units before the oscilloscope to enable some of the signal prior to the coincidence to be recorded. A total time interval of 20 ms is displayed on the oscilloscope.

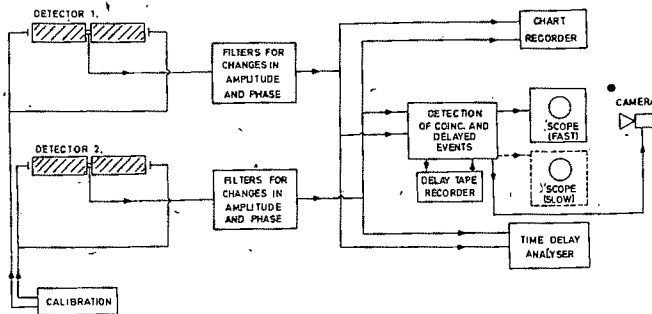


Fig. 4 Simplified block diagram of the data recording system.

A third method of recording data involves a system which measures time differences between nearly coincident pulses from the two detectors, using a 400-channel pulse height analyser operating in multiscaler mode. A pulse from one detector causes the analyser to sweep through its channels at a fixed rate. If a pulse occurs in the other detector, it is delayed by exactly half the total sweep time and then the number of counts in the channel at the sweep position is incremented. Thus at the end of a run the analyser automatically produces a time delay distribution.

Experimental Results

A result of limited accuracy can be obtained from the chart recordings alone. A short stretch of chart record (32 d) taken during September and October 1972 was analysed by scanning the trace for each detector separately and then searching the lists of pulse times for coincidences. The chance coincidence rate was determined by searching for delayed coincidences with displacements of 1, 2 and 3 h in the pulse times for either channel. Taking a coincidence window of 18 s and a two-detector 25% threshold of $0.6kT$ gave a coincidence rate above chance of 2.3 ± 2.1 per month of 28 d.

Many more precise and extensive data have been obtained using the electronic analysis systems.

The time delay distribution from the multichannel time analyser is shown in Fig. 5, for data taken over a period of 7 months, from September 1972 to April 1973. The upper plot covers delays from -2 to $+2$ s; the lower plot shows the central region on an expanded scale. There is no significant excess of pulses in the central region of the distributions, whereas tests showed that almost all short coincident pulses would have been recorded in the two central 10 ms bins. In those two channels we find an excess of 5 ± 11 counts in 150 d of running, corresponding to a rate of coincident pulses above the chance rate of 0.9 ± 2.1 month $^{-1}$ at a mean two-detector 25% threshold of $0.30kT$.

We now discuss data from the photographic recording system, over the same period of 7 months. The oscilloscope was triggered by pulses from the two detectors, above the discriminator thresholds, arriving within 6 ms of one another. The photographs were scanned and measured, and the pulse heights and time delay for each event were punched on to computer cards for subsequent analysis. Both prompt coincidences and coincidences with one signal delayed by 800 ms were analysed.

Analysis of the time delay distributions obtained from the

photographic records shows no significant peak at zero delay. Tests with artificial pulses near threshold indicate that about 85% of short coincident pulses would be recorded within a 1.6 ms time interval around zero delay, and we find that the numbers of events in the prompt and delayed distributions within this time interval are not significantly different. The number of coincident events above chance determined in this way is -1 ± 28 in 180 d, or -0.16 ± 4.4 per month. The mean two-detector 25% threshold for this result is about $0.27kT$, taking account of the 15% loss of coincident pulses which fall outside the central 1.6 ms time interval.

The pulse height information from the photographic records is also of interest, particularly in searching for rare coincident events. In Fig. 6a and b we show two-parameter plots of pulse heights from the two detectors for prompt and delayed coincidences. A short pulse of gravitational radiation would be expected to give a prompt coincidence with roughly equal pulse heights in the two detectors. Dotted lines are drawn at equivalent energies of $0.5kT$ for the two detectors, and most coincidences are seen to have energies less than this value in both detectors; a smaller number have energies greater than this value in one detector. There are two prompt coincidences and one delayed coincidence with energies greater than $0.5kT$ in both detectors. The delayed coincidence and one of the prompt ones are only approximately in coincidence, having time differences between the pulses on the two detectors of 3.8 and 5.3 ms, respectively. The remaining prompt coincidence, however, has a time difference of less than 0.5 ms. This is our best candidate for a true gravitational radiation event. It registered equivalent energies of 0.64 and $0.61kT$ on detectors 1 and 2, respectively, and was recorded on September 5, 1972, at 13 h 07 min 29 s UT.

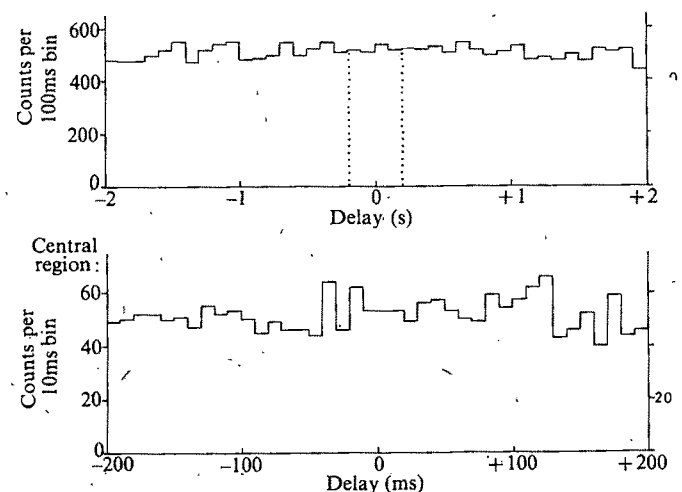


Fig. 5 Distribution of time delays between pulses from detector 1 and detector 2 for 7 months of observation (September 1972–April 1973). The 400 channels of the time analyser are grouped in tens in the upper plot, and the individual 10 ms channels for the central 400 ms (dotted lines in upper plot) are shown in the lower plot.

The photographic records contain a considerable amount of detailed information about the coincidence events, including the thermal vibration of the detectors, for 10 ms before and after the time of the coincidence. The photographic record for the event of September 5 is shown in Fig. 7. Here the top and bottom traces are the signals after bandpass filters F1, and show the thermally excited oscillations of the two detectors. The two central traces

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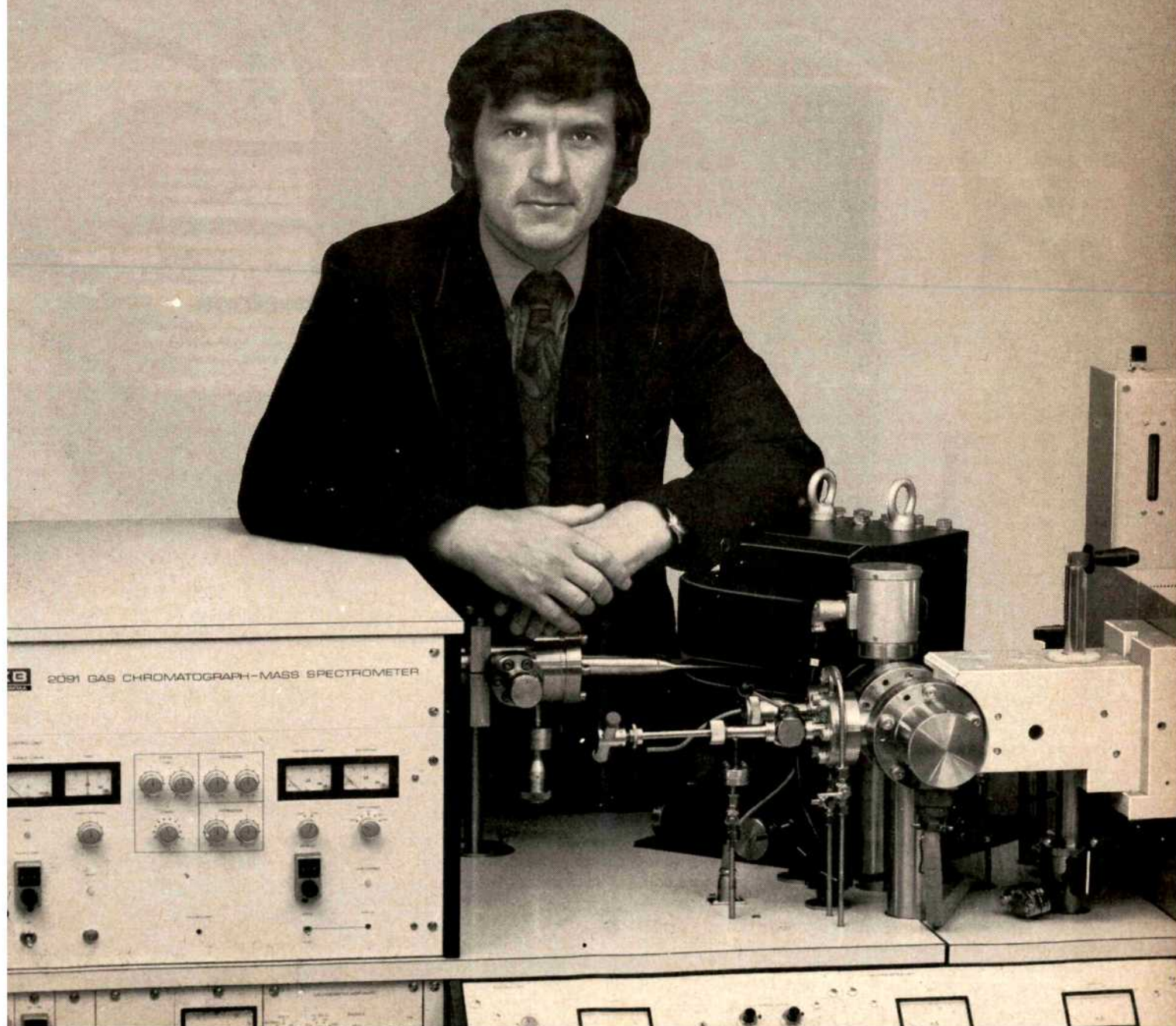
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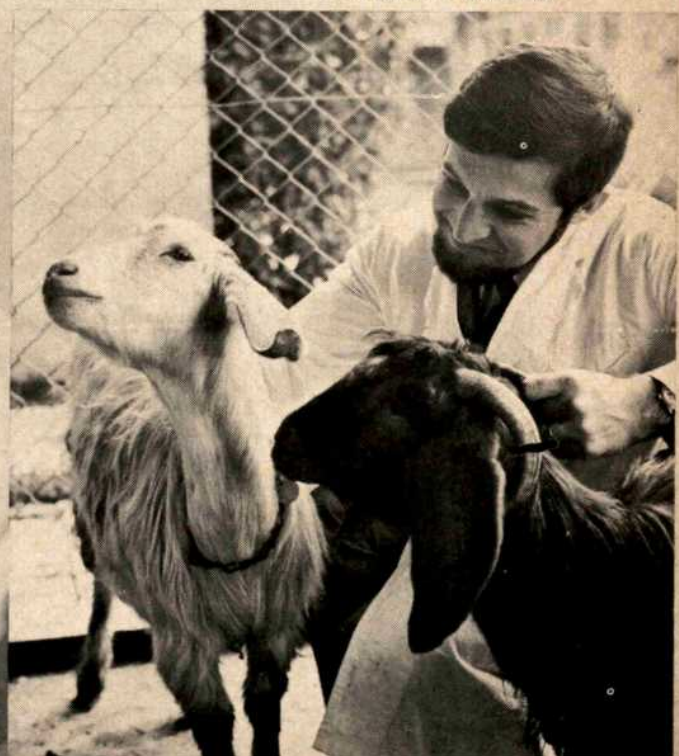
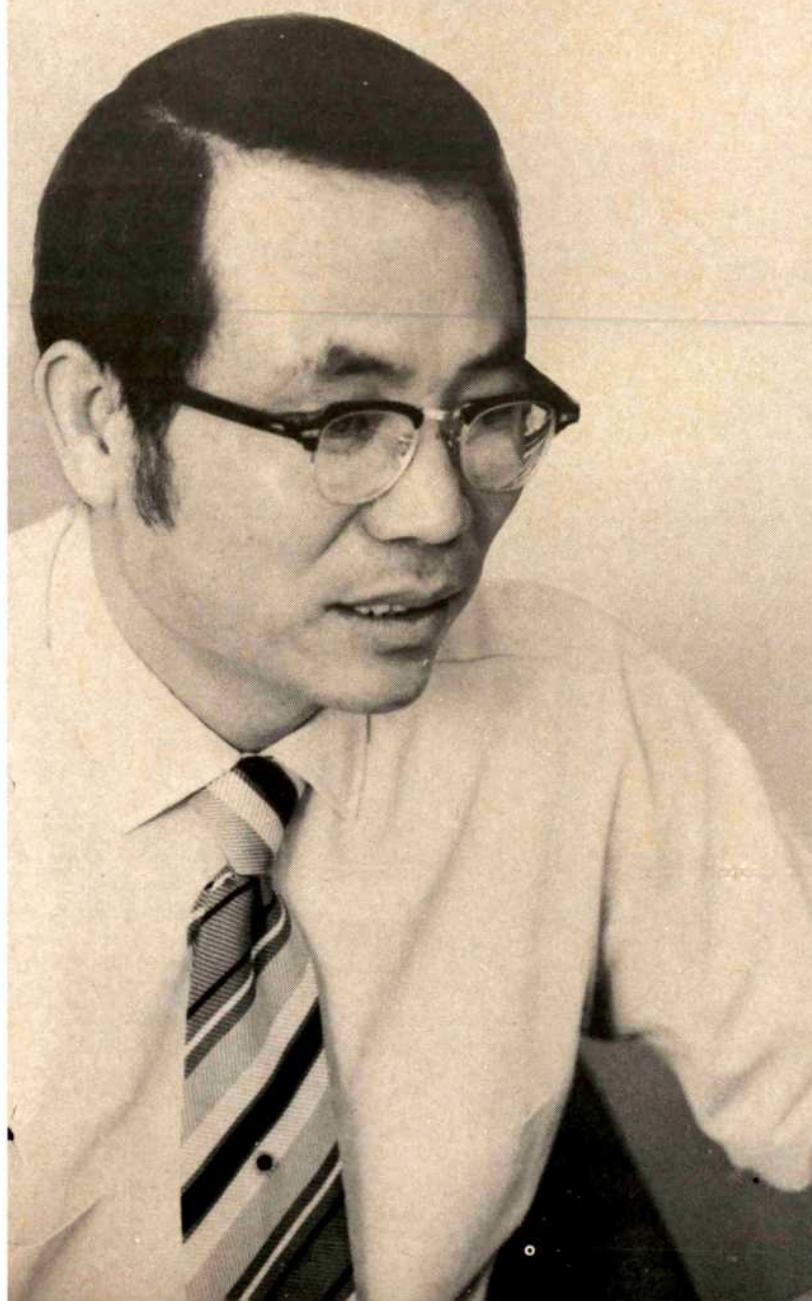
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0.12.748250.4

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Proceedings of the Third International Symposium on Yeast Protoplasts, held at Salamanca, Spain, in October, 1972

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0.12.722160.3

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0.12.350750.2

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December 1973, xvi + 388 pp., £8.20/\$23.00

0.12.435460.2

This work covers the areas of traditional experimental psychology in which theories are quantitative rather than qualitative. In each of these areas—human judgement, signal detection, reaction times, and learning—there are several different theoretical approaches which can be employed. This book presents the principal theories, paying particular attention to the ideas underlying each, and illustrates them with simple examples. At appropriate points, the theories are compared with each other, and with the experimental evidence, to see what conclusions are justified about their relative usefulness and applicability.

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are the same signals after the notch filters and indicate the forces acting on the detectors. (These signals do not represent the waveform of the force acting on the bar, however, since the filter used here was not a true inverse filter.) Important points to note are: (1) the signals on the central traces are in phase; (2) the signals on the central traces are similar in amplitude, waveform and duration, and correspond to a pulse of equivalent energy of about $0.63kT$, with a duration of less than 3 ms; (3) there is an evident change of amplitude of the top trace, and a less evident but equally significant change of phase of the bottom trace. Each of these changes is consistent with the corresponding signal from the notch filter. This shows that the signals arise from forces applied to the bars rather than from electrical interference in the amplifier or elsewhere.

To establish the significance of this event, we must esti-

mate the probability of obtaining a signal of this general character by chance. We have done this using the measured spectra and counting rates from each of the detectors near the time when the event was observed, and evaluating the rate expected for coincident pulses of amplitude equal to or greater than 0.8 of the amplitude of the signal seen on each of the centre traces of Fig. 7 and occurring within

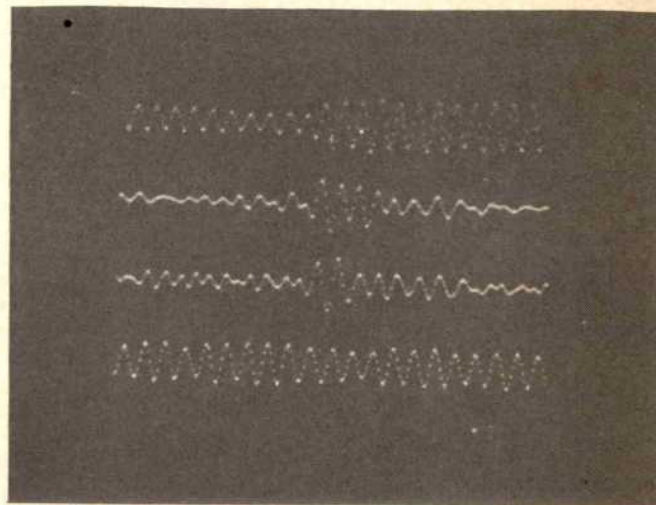


Fig. 7 Photograph of the event recorded on September 5, 1972, at 13 h 07 min 29 s UT.

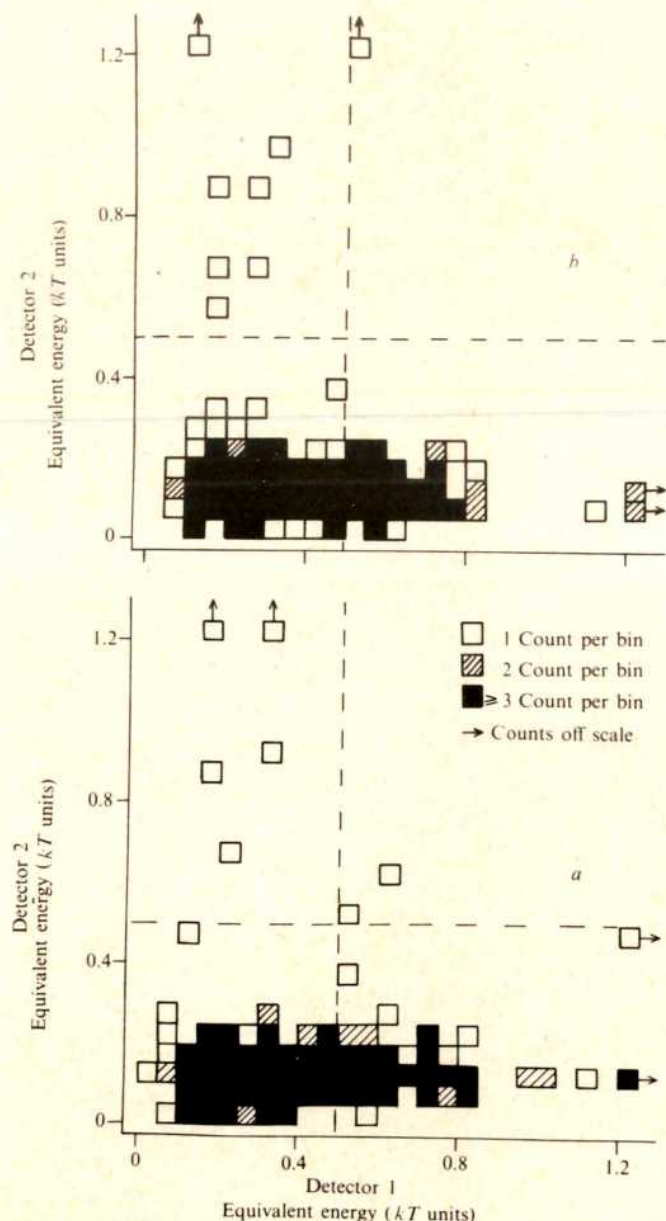


Fig. 6 Plots of equivalent pulse energies from the two detectors, for all coincident events within the 6 ms resolution time, for *a*, prompt coincidences; *b*, delayed coincidences. Data from September 1972 to April 1973. We note that there were slight changes in the noise levels of the detectors during the course of the experiment, altering the distribution of the pulses to some extent.

0.5 ms of one another. We find that one might expect one coincidence satisfying these criteria per 100 yr. Since these criteria are rather loose, it seems very improbable that the observed event is a chance coincidence of unrelated phenomena in the two detectors. At present we know of no experimental reason to reject the hypothesis that this signal was caused by gravitational radiation.

Comparison with Weber's Experiments

An unsuccessful search for gravitational radiation was reported about a year ago by Braginskii *et al.*⁷, with detectors of comparable sensitivity to those of Weber. Very recently, while the present paper was being prepared, null searches with single detectors have been reported by Tyson⁸, using a large and sensitive detector having, however, a pass band which did not overlap any of those of Weber's experiments, and by Garwin and Levine⁹ with a smaller detector of lower sensitivity.

Our present experiments were not designed primarily to confirm or refute Weber's observations, but the facts that our relatively wide bandpass does overlap one of Weber's experiments at 1,030 Hz (ref. 10) (where he observes the same number of coincidences as at 1,660 Hz) and that our apparatus is relatively sensitive, make it interesting to compare our observations with Weber's findings. This comparison is valid, however, only under the assumption that Weber's pulses are of short duration (a few milliseconds or less).

The signal analysis methods used in most of Weber's experiments and the lack of published data on energy calibration and pulse detection efficiency make it difficult to estimate precisely the energies of the gravitational radiation bursts which could be responsible for the signals he observed and the rate of bursts implied. However, it is possible to compare our experiment with one of Weber's in a simpler way. We take a particular energy of gravitational radiation pulse, and calculate an upper limit to the pulse detection efficiency

of Weber's experiment as determined by fluctuations in the thermal energy in the bar alone, for this size of burst. If we assume that the coincident signals reported by Weber were due entirely to gravitational waves of this energy, we can deduce a lower limit to the rate of occurrence of such bursts. Repeating the calculation for a range of energies, we can obtain a lower limit to burst rate as a function of possible burst energy. In our own experiments we have directly measured the detection efficiency for a wide range of applied force pulses, so for each assumed gravitational wave burst energy we can derive a rate of occurrence of bursts from our observed coincidence rate, and this can be directly compared with the corresponding lower limit to burst rate deduced from Weber's observations.

Weber has used various methods of analysis in his different experiments, but one set of data which is particularly amenable to this comparison is that obtained in the period May 20 to November 20, 1970, and presented graphically in Fig. 3b of ref. 2. The events plotted there were selected from the noise fluctuations registered on chart recorder tracings on the basis of two main requirements: (1) a coincidence circuit had indicated that the signals from the two detectors had crossed a certain threshold within 0.5 s of one another, and (2) the energy of each bar had exceeded another threshold for each bar, this threshold being defined by a condition that there be 100 crossings of the threshold per day. Either of these requirements could be used alone to set an upper limit to possible efficiency; we will use requirement (2). If we assume that the bar has mean thermal energy kT in the mode being studied, and that the quality factor of the cylinder is 70,000, then it can be deduced that the energy of the mode will exceed a threshold of $4.8kT$ 100 times per day. Additional noise from amplifiers or transducers can only increase the rate of crossing any given threshold, so we can take $4.8kT$ as a lower limit to the effective thresholds in this experiment.

An incident gravitational wave may either increase or decrease the energy of the cylinder vibration, and the sign and magnitude of the change will depend on the phase relationship between the gravitational wave and the bar, and the initial energy of the bar. For short gravitational wave bursts of given equivalent energy, the probability that the energy of the cylinder will exceed a threshold of $4.8kT$ within one bar damping time of the pulse can be calculated¹¹. For a simple threshold-crossing detection method we might take this probability as being a first approximation to the probability of detection of these gravitational pulses, or the "detection efficiency" of the detector. We find, for gravitational pulses of energy $3kT$, a detection efficiency of 0.3, for kT , a detection efficiency of 0.075, and for $0.3kT$, a detection efficiency of 0.020 for one of Weber's detectors. In a coincidence experiment a given gravity wave burst must be detected in both detectors so the efficiency of coincident detection cannot be higher than $(0.3)^2 = 0.09$, $(0.075)^2 = 0.0056$, and $(0.020)^2 = 0.00040$, respectively. The actual efficiency will be less than these values in practice, for (1) the presence of amplifier and transducer noise will decrease the efficiency for a given threshold crossing rate, and (2) the additional requirement of operating a coincidence circuit of relatively short resolving time cannot increase the detection efficiency, and may decrease it significantly.

The rate of observed coincidences above chance reported by Weber in the data under consideration is $0.75 \pm 0.07 \text{ d}^{-1}$. Taking the upper limits to coincidence efficiency just given, we find for gravitational waves of energy $3kT$ that the minimum incident rate of bursts is 7.5 d^{-1} , for kT it is 133 d^{-1} , and for $0.3kT$ it is $1,880 \text{ d}^{-1}$.

For our own present experiment, the coincidence efficiency for the two central 10 ms bins in the time analyser data was found by measurement to be 0.8 at $3kT$, 0.055 at kT , and 0.00021 at $0.3kT$. (The energies are those given to Weber's bar by the pulse in question.) Our observed coincidence

rate above chance is $0.03 \pm 0.07 \text{ coincidences d}^{-1}$. Thus our experiment gives an incident rate for gravitational wave bursts of $0.04 \pm 0.09 \text{ d}^{-1}$ for $3kT$, $0.6 \pm 1.3 \text{ d}^{-1}$ for kT , and $150 \pm 340 \text{ d}^{-1}$ for $0.3kT$.

All of our rates here are significantly smaller than the minimum corresponding rates of bursts implied by Weber's data, on the assumption that the sources of Weber's coincident signals are millisecond pulses of gravitational radiation. This simplified analysis does not itself show a contradiction between our results and Weber's provided that the pulses seen by Weber had energies of $0.25kT$ or less, and a corresponding rate of occurrence of 2,300 or more per day. A more realistic analysis would give an even lower efficiency for Weber's experiment, would require a larger incident rate and would extend the region of apparent discrepancy to still smaller pulses. If Weber's signals were due to pulses smaller than these, the total energy flux implied would be even larger than previous estimates have suggested.

Overall Implications

We have presented the results of seven months of operation of two wide-band gravitational radiation detectors. In this time we have observed one distinctive signal which fulfils the requirements expected of an event due to a short pulse of gravitational radiation, at a level which would give an energy of $0.63kT$ to each of our detectors, initially at rest.

In 1970 Weber reported detecting a flux of about 1 event d^{-1} (ref. 2). We have attempted to assess the performance of Weber's equipment in a way which gives an upper limit to its sensitivity, and have made a comparison with our experimental results. We conclude that it is unlikely that the signals reported by Weber in 1970 were due to pulses of gravitational radiation of duration less than a few milliseconds, assuming that the source has not changed significantly since then. But our present observations do not exclude the possibility that Weber may have detected bursts of gravitational radiation of much longer duration.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Laser Radar Observations of Atmospheric Potassium

LASER radar measurements of night-time atmospheric sodium are now an established technique; they have already made significant contributions to our knowledge of the distribution of sodium atoms in the 75 to 105 km height region¹⁻⁶, and have recently been extended into daytime⁷. It has often been the practice in airglow methods to study sodium, potassium and lithium simultaneously since their chemical and physical properties are similar, but, to date, no laser radar measurements of either lithium or potassium have been reported. We report here the result of an experiment to detect and measure the density and distribution of atomic potassium in the 76 to 100 km height region using a laser radar system.

A tuned dye laser was used to generate a resonance wavelength of potassium, 769.9 nm. The lasing medium was a solution of 3,3'-dimethyl-2,2'-oxatricarbocyanine iodide in ethylene glycol⁸, which was circulated through a cylindrical cell 50 mm long and 10 mm diameter and pumped, nearly longitudinally⁹, by a pulse from a Q-switched ruby laser. The tuning elements were two tilted Fabry-Perot etalons¹⁰ and a tuned solid etalon of 47% maximum reflectivity which was used as an output reflector. The laser spectrum was recorded on infrared plates using a grating spectrograph. The laser gave an output of about 40 mJ with a linewidth of the order of 10 pm. Because the column density of potassium was expected to be one hundredth of that of sodium and because the laser output and photomultiplier efficiency were lower than in equipment commonly used to study sodium, it was expected that the signal would be comparatively weak. It was therefore decided to use the large receiver, 15 m² collecting area, of the mark II laser radar system at Kingston, Jamaica, described by Kent, Sandland and Wright¹¹, and the dye laser was incorporated into this system.

In Table 1 we summarise the results of 600 laser firings. The photons were counted from altitudes between 31.5 and 35.5 km where Rayleigh scattering by the air would be expected to be dominant, between 75.5 and 99.5 km where resonance scattering by potassium should occur and Rayleigh scattering should be negligible, and between 103.5 and 151.5

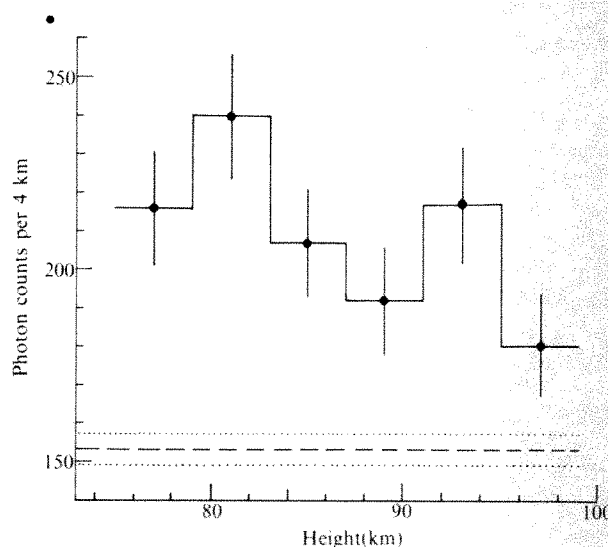


Fig. 1 Postassium return on January 25 and 27, 1973. The points are the scattered signal and background noise summed over 4 km height intervals. ± 1 s.d. of the count is indicated by the vertical error bar on each point. ---, Average background noise determined from measurement at heights of 103.5 to 151.5 km; ..., ± 1 s.d. of the background noise.

km where the counts should be a measure of the background noise. These noise counts have to be subtracted from the counts at lower altitudes to determine the signal. A highly significant signal of 334 ± 45 counts was obtained from 75.5 to 99.5 km. To prove that the signal was not due to a spurious source of noise, the laser was detuned and the result (Table 1) showed that the counts in the 75.5 to 99.5 km region were not significantly different from the measured noise. The data in Table 1 also show that the Rayleigh scattered signals were not the same in the two cases, due to a loss of output when the laser was detuned. Nevertheless, the measurement of January 27 gave at 75.5 to 99.5 km an excess of 0.117 ± 0.020 counts per Rayleigh count; when detuned a significantly smaller excess was obtained, -0.007 ± 0.047 counts per Rayleigh count. We conclude that resonance scattering from potassium was observed.

The effective total scattering cross section of a potassium atom for a laser linewidth of 10 pm is 1.6×10^{-16} m² so we

Table 1 Returned Signal for Different Operating Conditions

Operating condition	Date	Local time	No. of shots	Observed signal (Rayleigh return) + noise from 31.5 to 35.5 km	Observed signal* (potassium return) + noise from 75.5 to 99.5 km	Background noise* adjusted to 24 km gate†
Laser tuned to 769.9 nm	January 25, 1973	0040-0330	200	160‡	378 ± 20	246 ± 19
	January 27, 1973	0230-0520	400	1,836	876 ± 30	674 ± 18
	Total		600	1,996	$1,254 \pm 36$	920 ± 27
Laser detuned	February 1, 1973, to February 2, 1973	2220-0433	600	863	911 ± 30	916 ± 15

* The errors given are ± 1 standard deviation.

† Various gate widths used.

‡ Receiver shutter only partly open

estimate that the column number density of potassium atoms on January 27, 1973, was $9 \times 10^{11} \text{ m}^{-2}$. This density is consistent with twilight photometric data¹²⁻¹⁴.

Figure 1 shows the resonance scattering profile for the heights 75 to 100 km. There is a broad potassium layer with appreciable density over the whole of the 24 km region studied. The height is consistent with twilight data¹²⁻¹⁴, but the large fraction of potassium that is below 84 km is different from that of sodium in the profiles obtained at 51° N (ref. 15) or at 23° S (ref. 6). This may be a consequence of differences in the chemical and diffusive equilibria of sodium and potassium or it may be that sodium was also at a lower height at Jamaica (18° N) on this occasion compared with that measured previously at other latitudes.

It is hoped to extend these measurements to provide a greater height coverage and finer resolution. Comparison with nearly simultaneous sodium profiles will also be attempted.

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Tidal Friction

It seems worth while to compare various estimates of the secular accelerations of the Moon's mean motion ($\dot{n}$) and the Earth's rate of rotation ($\dot{\omega}$), and also of the dissipation (dE/dt) in the M_2 oceanic tide. I have recalculated the values given in chapter 8 of ref. 1, and I indicate the consequences of various other estimates in Table 1.

Van der Waerden's value² from ancient observations (back to the ancient Greeks) was found by classifying the data into four intervals. The number of degrees of freedom is therefore small, and a considerable error was more likely than the apparent uncertainty would suggest. In ref. 1 I made some adjustments, which have been further modified to give the result in Table 1. Newton's and Stephenson's values (refs 3 and 4 respectively) are based on much work, but differ rather

seriously, particularly in the results that they give for the apparent secular acceleration $v (= \dot{n} - \dot{\omega}/27.3)$.

Under 'modern observations' the value of n from van der Waerden is essentially that of Spencer Jones, which eliminates variation of $\dot{\omega}$ in the past 250 yr. I have calculated $\dot{\omega}$ and dE/dt from it on the supposition that the angular momentum in the Earth-Moon system and the Earth's moment of inertia are constant. Spencer Jones's uncertainties may have been underestimated (see ref. 10, page 400). Newton's satellite value⁵ is based on perturbations of artificial satellites by the potential due to the tides; he gives the lunar contribution to $\dot{\omega}/\omega$ and I have calculated $\dot{n}$ and dE/dt above from it. The value of $\dot{\omega}$ calculated from $\dot{n}$ would be increased numerically by allowance for the solar tide and reduced by the thermal atmospheric tide. It seems clear that $\dot{\omega}$ varies, and only an average value means much, but there is no apparent reason why $\dot{n}$ should have varied appreciably in the past 2,000 yr.

Table 1 Consequences of Other Estimates

Author	$-\dot{n}$ (1" cy ⁻²)	$-\dot{\omega}$ (1" cy ⁻²)	$-dE/dt$ (10 ¹⁹ erg s ⁻¹)
Ancient observations			
Van der Waerden ²	17.9 ± 1.1		
Newton ³	42 ± 4	1,180 ± 140	
Stephenson ⁴	34.2 ± 1.9	1,213 ± 57	5.1
Modern observations			
Van der Waerden ²	22.4 ± 1.8	1,198 ± 96	2.76 ± 2.2
Newton (satellites) ⁵	23.5 to 17.5		2.88 to 2.16
Van Flandern ⁶	52 ± 16		
Tidal theory			
Munk and MacDonald ⁷			3.2
Pekeris and Accad ⁸			6.3
Hendershott ⁹			2.7

Van Flandern⁶ studied occultations, using an atomic standard of time, and consequently his result does not depend on the rotation of the Earth. It covers, however, only a short interval of time and will probably be improved. Pekeris and Accad⁸ made a numerical solution for the M_2 tide, using the actual form of the oceans. They did not allow for the elastic yielding of the solid Earth, and their dissipation should probably be halved. Hendershott's solution⁹ allows for it. It seems probable therefore that the rate of dissipation in the lunar semidiurnal tide is about $2.7 \times 10^{19} \text{ erg s}^{-1}$, and this is consistent with Spencer Jones's $\dot{n}$ and Newton's value from artificial satellites. It seems to me that these are the least likely to be affected by disturbances not yet considered. This is substantially greater than my estimate for the dissipation in ref. 1. To find these I started with a wholly provisional estimate (page 308) of the apparent secular acceleration of the Moon, and neglected tidal dissipation along the open coasts, which is probably much larger than was thought (page 313).

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Anellotubulates are Manufactured 'Microfossils'

IN a world where fossil names become ever more prolific, it is unusual to have the opportunity to reverse the trend. Anellotubulates, "an independent morphologic group of organisms", were first described by Wetzel^{1,2} and later placed by him in the family Mikrocallycidae³. There followed a detailed publication by McLachlan⁴, describing world-wide occurrences of anellotubulates and giving a detailed morphological description of these 'fossils'.

Anellotubulates 'ring-tubers' are tubes of constant or varying diameters, often having characteristic annular thickenings and sometimes a thecal form or termination (Fig. 1). They range up to approximately 1 mm in length and 0.5 mm in diameter. The outer surfaces are creamy white and are often rough. The inner surfaces are smoother and sometimes stained brown. They are well figured by McLachlan⁴ who shows most variations. They are amorphous and electron probe microanalysis indicates iron and phosphorus as principal elements in their composition.

Anellotubulates, although not described as such, had been found by several geologists in Britain, including J. E. Pollard and R. E. Elliott in the early 1960s. They considered the possibility that these structures were microfossils but concluded that they were contaminants. The source of contamination was not identified and the work was not published, but a link between the occurrence of these structures and the use of hydrogen peroxide in the preparation of samples for microfauna was established. Anellotubulates often occurred as encrusting forms on fragments of shale disaggregated by hydrogen peroxide. We became interested in this problem in 1972 when anellotubulates were found in microfaunal preparations of Coal Measures mudstones.

Our experience was the same as that of the earlier British workers, in that anellotubulates were found only when hydrogen peroxide was used in the preparation of samples. This fact together with the world-wide distribution of these 'fossils' at stratigraphic horizons varying from Carboniferous to Cretaceous, and their apparent disregard for any particular ecological niche, reinforced in us the suspicions of earlier workers.

Contamination of samples by living organisms either at source or during processing was considered and rejected, for although anellotubulates bear a superficial resemblance to parts of lichens and fungi, no modern species was directly comparable. Experiments introducing modern lichens into the normal preparation of microfaunal samples using hydrogen peroxide failed to mineralise the plant structures. Contamination of hydrogen peroxide by living organisms during its production or afterwards was discounted because of its inhospitable nature.

We suspected that an inorganic source was the most likely origin for these structures, and that they might be produced as artefacts during the reaction between hydrogen peroxide and rocks containing finely disseminated pyrite. A simple experiment proved this to be correct. A piece of Coal Measures shale containing finely divided pyrite was placed in a watchglass and immersed in 100 vols hydrogen peroxide (commercial grade). Observations under a binocular microscope indicated the following sequence of events. Bubbles accumulated on the shale, originating on and below the surface, eventually leading to streams of bubbles as the reaction proceeded. After a period varying from a few minutes to several hours a transparent to white gel-like deposit appeared around the edges of streaming bubbles. Where bubble streaming was persistent, we observed that the deposit formed a tubular growth around and parallel to the bubble stream, the internal diameter of the tubes being directly related to that of the emergent bubbles, and that the original gel-like deposit appeared to harden around the bubble stream, enabling the deposit to build up into a tube-

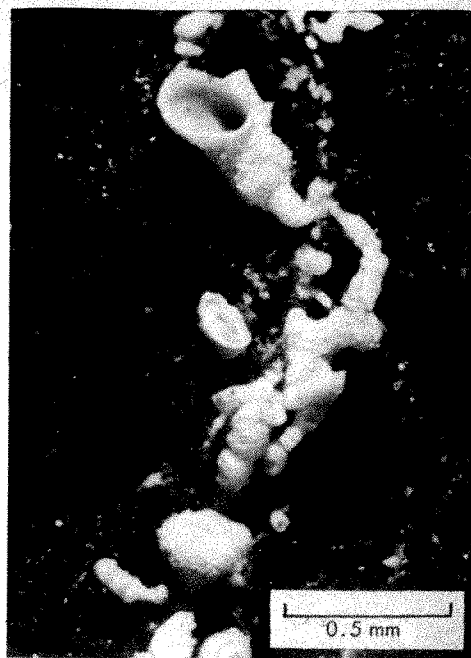


Fig. 1 Anellotubulates grown on carbonaceous Coal Measures shale soaking in 100 vols hydrogen peroxide. Upper centre, large specimen showing early narrow tube swelling into a distorted trumpet form with smooth interior and pronounced rim. After growth a slow stream of expanding bubbles was observed being released from the wide aperture. Left centre, short trumpet form with partially blocked distal end and slit-like aperture. Right centre-lower centre, adherent, constricted and inflated tubes attached along a pyrite-rich layer in shale. These tubes show a white granular external surface. Lower left, narrow tube expanding into a short cylindrical tube.

like growth. As the tube hardened at its base, constricting the diameter of the bubbles, the softer, upper portion of the tube expanded, conforming to the increasing circumference of the bubbles. Trumpet-shaped tubes, formed by this process, were common. Vermiform tubes of an even diameter were also produced. A typical assemblage is seen in Fig. 1. Variations in the quantity of gas produced, and in bubble diameter, resulted in tubes of variable diameter. The hardening of the tubes, while still immersed in the reagent, was progressive and after several hours they were quite brittle.

Production of these artefacts would seem to be dependent on the type of hydrogen peroxide used. Enquiries revealed⁵ that phosphates are often used as stabilising agents in hydrogen peroxide. Commercial and pharmaceutical grades contain as much as 100 or more times the amount present in analytical grades. In our experiments tubes could not be consistently produced using commercial or pharmaceutical grades of hydrogen peroxide, though all tubes that were manufactured were made with these grades. Analytical grade hydrogen peroxide never produced tubes, and this prompted the idea that phosphate in hydrogen peroxide was the source of the phosphorus found in anellotubulates. This idea was reinforced when it was found that if sodium hexametaphosphate was added to hydrogen peroxide abundant tube growth took place. Using sodium hexametaphosphate, tubes were produced on limestone, dolerite (Whin Sill), garnet-pyrite vein rock associated with Shap Granite, and Carboniferous mudstone.

The tubes produced in our experiments embrace all the shapes previously described for anellotubulates, and seem to have the same chemical composition. Those formed without the addition of sodium hexametaphosphate fall within the size range described by Wetzel³ and McLachlan⁴, but much larger tubes are produced when this chemical is added.

Hydrogen peroxide reacts in the breakdown of samples by oxidising any pyrite present. The chemistry of the reactions, which result in the gel, probably an iron phosphate, being deposited around areas of oxidising pyrite, is still under investigation. There would seem, however, to be little doubt that the elements forming anellotubulates are obtained from the iron of pyrite and the phosphorus of the hydrogen peroxide stabiliser.

The consistent reproducibility of shapes in an amorphous compound during a chemical reaction is an interesting phenomenon. Our research to date would indicate that the iron phosphate is deposited as a gel which seems to have adherent and elastic properties, and which hardens progressively as the reaction proceeds. The streaming bubbles—probably of oxygen—would seem to act in two ways; in distributing the iron from its source at the pyrite to the site of its reaction with the phosphate, and also in physically moulding the gel. That these factors are interrelated is indicated by the final dominance of certain forms as a result of the normal course of this reaction. Assuming that the phosphate is available in decreasing amounts until exhausted during the reaction, the characteristic ring-like thickenings probably relate to periodic fluctuation in the availability of iron from the pyrite source.

We have, therefore, no doubt that anellotubulates can be manufactured as inorganic artefacts, and are led to suspect that all such 'fossils' described in the literature have been so produced. One discrepancy remains to be explained, however. This is a record by McLachlan⁴ of anellotubulates recovered from Australian Triassic sediments using monochloroacetic acid in one case, and boiling water in another, as disaggregating agents. The anellotubulates were apparently recovered by these means by P. J. Jones of the Bureau of Mineral Resources, Canberra, in 1966 and donated to McLachlan in 1971. We have been unable to produce tubes by either of these methods nor can we explain their production during the breakdown of rocks by these means.

We thank Dr M. A. Calver, Mr B. J. Taylor, Mrs Brenda Coleman, Dr J. Esson, Mr G. A. Sargeant, Dr R. E. Elliott and Mr I. R. McLachlan, for advice and help.

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Flocculation of Suspended Sediment in the Sea

INORGANIC sediment suspended in the sea is unstable as single mineral particles and occurs as flocculated aggregates with settling speeds many times greater than that of the constituent grains. This has been demonstrated both through observations of natural samples¹⁻⁵ and through laboratory experiments^{6,7}. In near-shore waters with high concentrations of terrestrially derived mineral matter the transport and deposition of fine sediment are greatly affected by flocculation. The exact

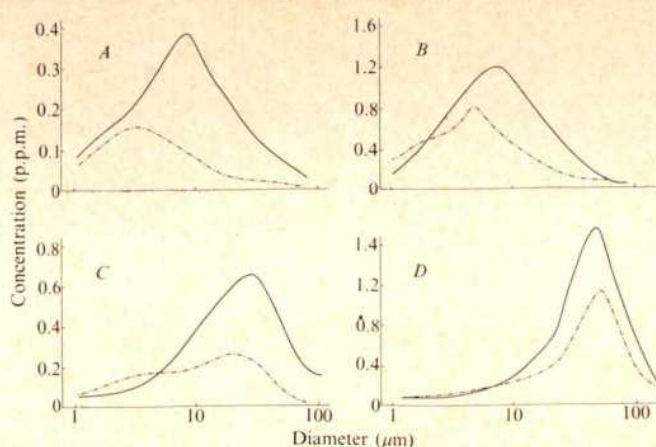


Fig. 1 Typical grain size spectra of particulate matter from coastal waters with high inorganic content. The solid curves show the natural distributions and the broken curves the deflocculated inorganic grains. Origin of samples: A, Northumberland Strait; B, Bay of Fundy; C and D, Petpeswick Inlet.

mechanism of floc formation in the sea is not well understood. The concentration, mineralogy and grain size of the suspended particles and the salinity, turbulence and temperature of the water are commonly regarded as controlling factors^{8,9}. Flocculated aggregates composed largely of organic matter have been observed in the sea^{10,11} and organic matter may be an important ingredient in the flocculation of inorganic sediment.

To determine the nature and mode of formation of inorganic flocs, the concentration, grain size and general nature of the suspended particulate matter in over 500 samples from a variety of coastal environments have been studied. Samples of seawater were collected with Niskin bottles or with a weighted surface sampling bottle. The samples were stored cold and dark and analysed as soon as possible but always within a few days of collection. An inverted phase contrast microscope was used for qualitative identification of the particulate matter. The size and concentration of particles between about 1 and 100 μm were measured with a model T Coulter Counter and the results plotted as particle spectra showing the equivalent spherical diameter of the particle volume relative to concentration in parts per million (p.p.m.)^{12,13}.

Under the microscope flocs appear as irregular masses or clumps of numerous individual grains. Occasionally whole planktonic cells (or parts of a cell) and other organic debris are included but most of the aggregates consist of smooth transparent sub-rounded mineral grains. The flocs form the largest particles in all samples but also range down to minute aggregates of the smallest grains. They are composed of an unsorted mixture of large and small grains. Individual grains not forming part of flocs also occur. These are more abundant among the larger grains and the largest grains in a distribution never seen to become part of a floc.

When gently shaken the bigger flocs move about and consist of a relatively low density, soft, jelly-like, loose network of grains. This conforms with Berthois's description¹ of aggregates of grains surrounded by a fine veil of organic matter.

Flocs were observed in all samples and formed the majority of particles in samples from highly turbulent areas, such as tidal inlets and narrow straits, and from near the bottom in regions of muddy sediment. The samples from these waters, high in inorganic sediment when analysed by Coulter Counter, were characterised by regular, almost symmetrical, broad distributions with well developed modes (Fig. 1). Total particle concentrations in the flocculated samples varied from 0.5 to 20 p.p.m. and modes usually ranged between 6 and 50 μm .

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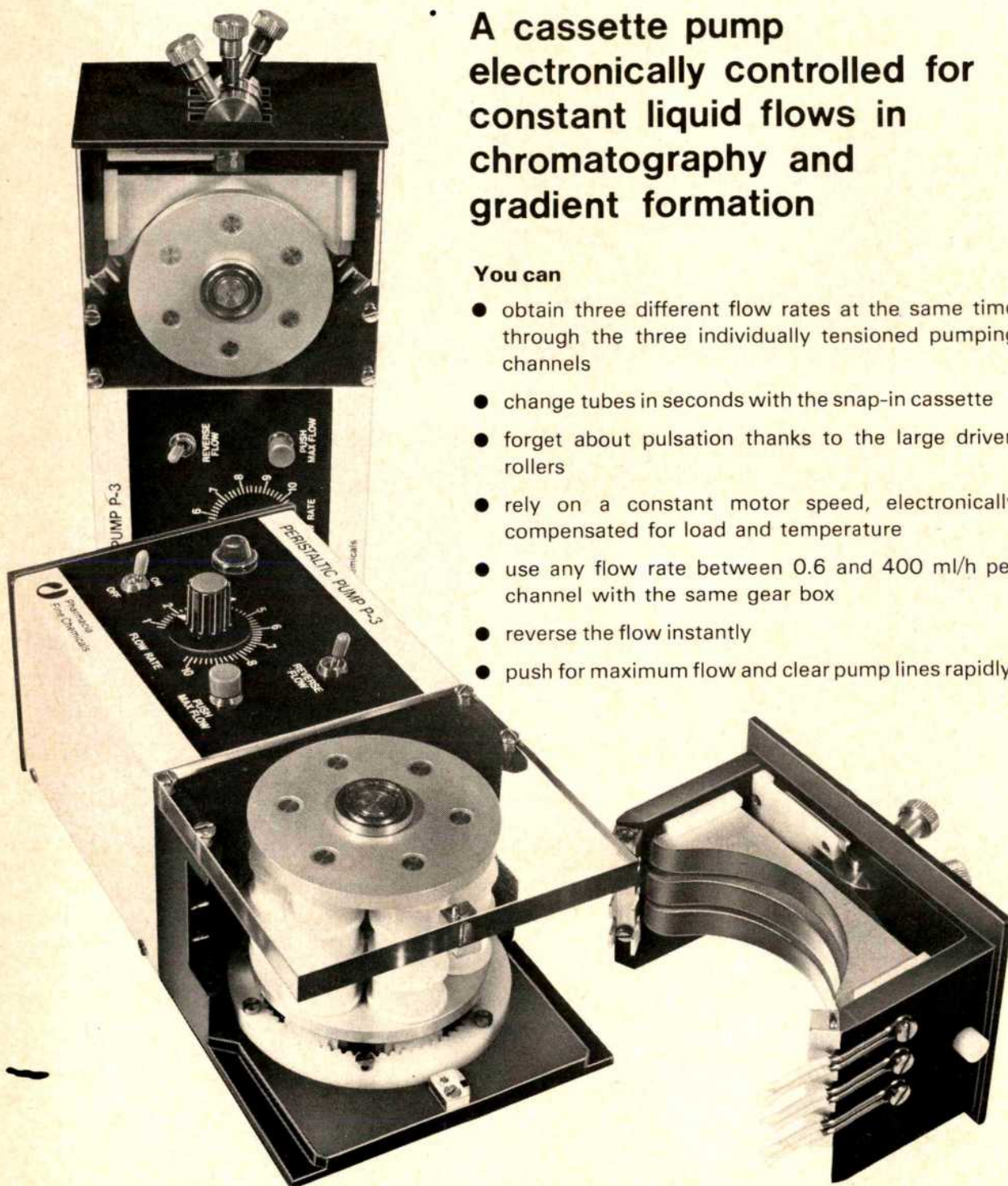
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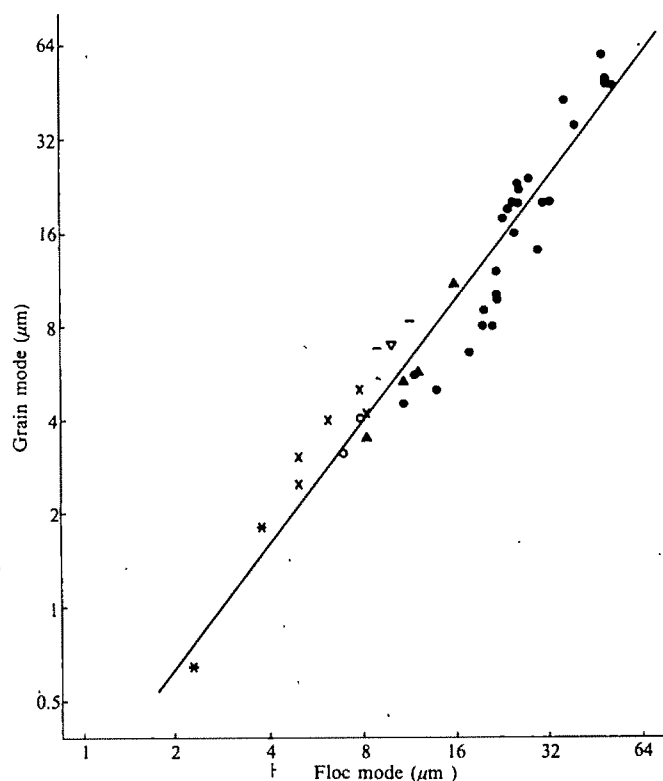


Fig. 2 Relationship between grain size mode and floc size mode ($r=0.941$, $P<0.001$). *, Artificially flocculated samples; ●, Petpeswick Inlet; ▲, Northumberland Strait; —, St. Margaret's Bay; ○, Nova Scotia Shelf; ×, Bay of Fundy; ▽, Chedabucto Bay.

These normal distributions seem to be a permanent stable state of thoroughly flocculated samples in which no further flocculation occurred. Vigorous agitation of samples did not change the size distribution; and the suspended floc mode as measured immediately after sampling did not change after storage for several months, during which time the particles settled on the bottom of the container in large lumps or rollers.

The sizes of the inorganic constituent grains forming the flocculated masses were measured as follows. About 500 ml of sample was filtered on to a Millipore filter and ashed in a Tracerlab low temperature ashers. This oxidised the filter paper and organic particles. The residue was wetted with 2% Calgon solution and then resuspended in particle-free 3% saline solution prepared by repeated filtering until the particle concentration was <0.005 p.p.m. The samples were deflocculated by ultrasonic vibration with the probe tip of an Artek Sonic Dismembrator for 1 min at a setting of 90. A microscope was used to check for incomplete dispersion or reflocculation of the inorganic particles before analysis.

When the samples were deflocculated the size spectra changed to a broader flatter distribution, usually slightly negatively skewed. The total particle volume was reduced by about half probably as a result of the loss of porosity or organic material or both. The most remarkable change in the spectra was a change in the mode, relative to the size of the original mode. The grain mode of the samples analysed is shown in Fig. 2 as a function of the original floc mode. The points from the natural samples in Fig. 2 fit the regression equation $\log(\text{grain mode}) = -0.578 + 1.295 \log(\text{floc mode})$.

There was no relationship between the mode size and the concentration of particulate matter, nor did any difference in mineralogical composition between the samples or in the salinity and temperature of the seawater, because of their varied sources, seem to have affected the flocculation process. A distinct relationship was noted, however, between mode size and current speed of the water at the place of collection. Samples with modes below about 14 μm came from the turbid

bottom layer of the shelf or from sheltered smaller bodies of water and, in the case of the Bay of Fundy, from close to the shore during slack tide. The samples with large modal size were collected from a narrow inlet with strong tidal currents where, during sampling over a tidal cycle, the mode size varied regularly with changes in the tide. The correlation between floc mode and dynamic conditions is not surprising in view of the dependence of grain size on turbulence¹⁴.

From the above observations it seems that in seawater particles flocculate into characteristic stable size distributions, the modes of which are determined by the initial size of the constituent grains. Flocculation of particles depends on two factors: particle collision during transport and adhesion of particles on contact^{15,16}. Fulfilment of the second condition has been demonstrated by many workers who have shown that in salinities above about 3‰ most fine sediment flocculates readily^{6,7}. I propose the following general mechanism whereby particle collisions transform a suspension of single grains of varying sizes into a permanently flocculated distribution.

Particles of different sizes will respond differently to gravity and turbulent forces. In the initial unflocculated suspension this will cause a random variation in grain speed and direction accompanied by abundant particle collisions. Because of their larger relative surface area and proportionally greater adhesive force the smaller particles flocculate most rapidly¹⁷. Larger grains may not be sufficiently surface active to flocculate with other single grains but they do adhere to the soft irregularly shaped flocs composed of many smaller grains. As progressively larger flocs are formed the transport velocities become more uniform and particle collision less frequent. Eventually a state is reached in which the transport velocities of the largest flocs equal the velocities of the largest grains and further flocculation ceases.

In the sea, particles are suspended in a turbulent medium with local velocity gradients and fluctuations. The forces acting on a particle change constantly and it may be that the stage at which all particles have the same dynamic transport velocities is never achieved. As flocs become larger they are subject to more shear stress and become more unstable, and a bigger increase in grain mode is required to produce a given increase in floc mode. This explains why the ratio of floc mode to grain mode decreases with increase in particle size (Fig. 2).

To test the sequence of flocculation in a sediment suspension a sample of fine glacial clay was dispersed in 3% NaCl solution

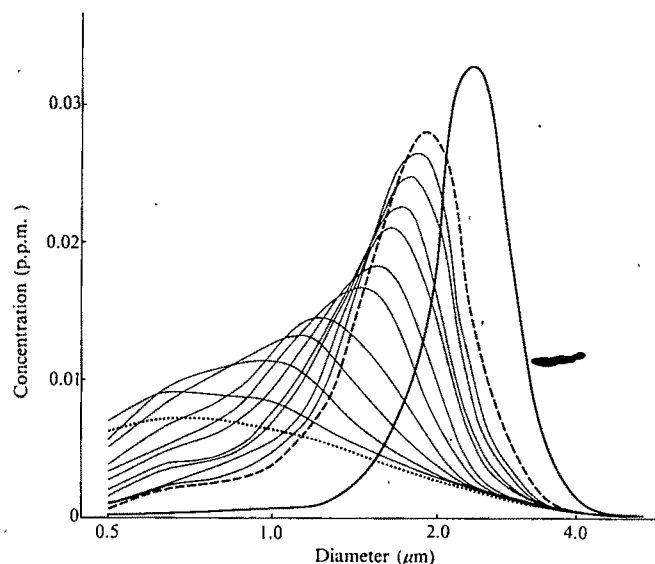


Fig. 3 Progressive flocculation of sediment stirred in 3% NaCl shows the final distribution (18 h) and the distribution measured every 0.5 h during the first 6 h. . . ., 0 h (initial); ---, 6 h; —, 18 h (final).

and stirred continually. Periodic measurement of the grain size shows (Fig. 3) that flocculation proceeds as a front along the distribution, involving progressively larger grains. After 18 h the suspension stabilised in a broad distribution similar to those formed by natural flocs. Further stirring resulted in a decrease of particle concentration probably on account of the adherence of the surface active particles to the walls of the glass container; there was, however, no further change in mode. The final stable mode conforms to the condition of stable flocculation illustrated in Fig. 2. The artificially produced floc distributions appeared identical, optically, to the natural distributions and it may be concluded that the experiment simulated floc formation in nature. The other datum point in Fig. 2 for artificially flocculated samples was similarly derived from a sediment sample stirred in clean seawater. So far no thoroughly flocculated suspensions with modes larger than 4 μm have been produced in the laboratory, possibly because of some deficiency in the organic matter required to duplicate the natural grain surfaces.

I thank R. W. Sheldon for discussions.

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BIOLOGICAL SCIENCES

θ -bearing Lymphocytes in Nude Mice

MICE homozygous for the mutation *nude* (*nu/nu*) are hairless¹ and deficient in thymus²⁻⁴ and thymus-derived (T)^{5,6} lymphocytes. They are generally referred to as being athymic and are widely used in immunology as a source of B lymphocytes uncontaminated with T cells, although there is evidence that the thymus is present, but is small and dysplastic^{3,4}. Indirect evidence has suggested that at least some nude mice have small numbers of T cells⁷⁻⁹, but this has been controversial. I report here the direct demonstration by immunofluorescence of a small population of θ -bearing cells in lymph nodes and spleens of nude mice using fluorescein-conjugated anti- θ antibody.

Anti- $\theta\text{C}_3\text{H}$ antiserum was prepared by immunising AKR mice with 10^7 C_3H MLV-Moloney lymphoma cells weekly for 6 weeks, followed by a further three boosts with 10^7 lymphoma cells and 10^7 C_3H thymocytes. The last inoculation included 4×10^6 Sarcoma 37 cells to induce ascites fluid which was collected 10 d later. Following heat inactivation for 30 min at 56°C , the immunoglobulin was precipitated with 40% saturated NH_4SO_4 and conjugated with fluorescein isothiocyanate¹⁰. After absorption (twice with 50% (v/v) packed AKR thymocytes) to remove autoantibodies, the conjugate used neat or diluted 1:2 (see below), labelled 100% of thymocytes and 35-40% of nucleated spleen cells of Balb/c and A mice, both of which express the $\theta\text{C}_3\text{H}$ allele, but did not label any cells in thymus or spleen of AKR or A/ θ AKR mice (Table 1), which carry the other θ allele, θ AKR. (A/ θ AKR are congenic mice differing from A only at the θ locus.) Absorption with A brain, but not A/ θ AKR brain, completely eliminated the fluorescence labelling activity of the conjugate, further confirming its specificity for $\theta\text{C}_3\text{H}$ (ref. 11).

Six nude mice from three different sources were studied (Table 1) and in each animal no obvious thymus tissue could be seen at the time of killing. Their lymph nodes (inguinal, axillary, brachial, mesenteric, deep and superficial cervical) and spleens were teased in RPMI 1640 medium with 20 mM HEPES buffer and 10% foetal calf serum, passed through a short column of glass wool and washed twice. Spleen cells were freed of erythrocytes by treatment with Tris-buffered NH_4Cl (ref. 12). Twenty microlitres of cells ($4 \times 10^7 \text{ ml}^{-1}$) was incubated with neat conjugate for 30 min at 20°C or 37°C , washed twice and examined under a coverslip with a modified Vickers M41 Photoplan fluorescence microscope, using incident blue-violet light or transmitted phase-contrast illumination¹³.

Between 0.2 and 1.6% of nucleated cells from lymph nodes and spleen of each nude mouse showed surface fluorescent staining (Table 1). Approximately 50% of the labelled cells appeared to be medium or large lymphocytes while the remaining 50% looked like small lymphocytes. As previously described with fluorescein-conjugated anti- θ antibody¹³, labelled cells always showed continuous smooth ring fluorescence, even when labelling was carried out at 37°C .

The specificity studies on the anti- $\theta\text{C}_3\text{H}$ -fluorescein conjugate (Table 1) make it clear that the labelled cells seen in nude lymphoid tissues were θ -bearing. Although epidermal cells¹⁴, fibroblasts (P. Stern, unpublished), and as yet unidentified cells in the central and peripheral nervous system¹¹ are known to express θ on their surface, in cell suspensions of lymphoid tissues, only thymocytes and T lymphocytes have been shown to be θ^+ , while B cells, granulocytes, macrophages, reticular cells and erythrocytes are θ^- (refs 6, 7, 11, 15, 16). This, together with the morphological appearance of the labelled cells by phase-contrast microscopy, makes it likely that the θ^+ cells were T lymphocytes. This is consistent with previous indirect evidence for the presence of small numbers of cells with T lymphocyte properties in nude mice⁷⁻⁹.

What is the origin of the θ^+ lymphocytes in nude mice? Since maternal cells crossing the placenta would have an unusually high probability of surviving in an immunologically incompetent nude mouse^{17,18}, the θ^+ cells could be of maternal origin; although rigorous attempts to demonstrate passage of cells from mother to foetus in mice using chromosome markers have generally failed¹⁹, Di George has referred to a child with thymic dysplasia having 2% maternally derived cells in its blood²⁰. It is unlikely that θ^+ lymphocytes could come from normal (+/+) or heterozygous (*nu*/+) littermates as placentae in mice are rarely fused²¹. In view of recent evidence that θ^- cells in mouse bone marrow and spleen can be induced to express θ by *in vitro* incubation with a soluble extract from mouse

Table 1 Percentage of θ -bearing Cells in Control and Nude Mice as Detected with Anti- θ C3H-Fluorescein

Mice	Tissue	Cells scanned*	No. labelled	% labelled
Balb/c	Thymus	200	200	100
	Spleen	200	78	39
A	Thymus	200	200	100
	Spleen	200	72	36
A/ θ AKR†	Thymus	10,000	0	0
	Spleen	13,000	0	0
AKR	Thymus	15,000	0	0
	Spleen	12,000	0	0
OLAC Nude 1‡	Lymph node	4,000	60	1.5
	Spleen	3,000	24	0.8
	Lymph node	6,900	36	0.5
	Spleen	7,200	37	0.5
	Lymph node	1,500	24	1.6
	Spleen	14,000	48	0.3
Nude/C57Bl/6 1§	Lymph node	19,500	100	0.5
	Spleen	22,000	90	0.4
	Lymph node	20,000	220	1.1
	Spleen	13,000	43	0.3
Nude/Balb/c¶	Lymph node	5,200	23	0.4
	Spleen	17,000	28	0.2

* Cells were scanned for surface fluorescence with a $\times 100$ oil immersion objective under blue-violet light and the total number of cells scanned was estimated by counting cells under phase contrast in one out of every ten fields examined.

† A/ θ AKR are congenic with A, differing only at the θ locus, and were originally obtained from Dr E. A. Boyse.

‡ Mice were purchased from OLAC (Southern) Ltd (Bicester), where they were produced by mating homozygous males (nu/nu) with heterozygous females ($nu/+$) and reared under specific pathogen-free (SPF) conditions. They were all females and 6–8 weeks old when used.

§ Mice were obtained from Dr I. Lefkowitz, of the Basel Institute of Immunology. They were both males, 10–12 weeks old, reared under SPF conditions and were produced by mating heterozygous ($nu/+$) males (in their eighth backcross generation on to a C57Bl/6 background) with heterozygous ($nu/+$) outbred NMRI females.

¶ Mouse was obtained from Dr L. La Fleur, of the Basel Institute of Immunology, who purchased it from G. L. Blomholtgård Ltd (Ry, Denmark). This nude was a 6-week-old female from a stock that has been backcrossed for 3–5 generations on to a Balb/c background.

thymus²², it is conceivable that θ^+ lymphocytes can develop outside the thymus, perhaps, in nude mice, under the influence of thymus humoral factors derived from normal littermate⁸, maternal or even dysplastic nude thymus tissue *in utero*. Finally, it is possible that θ^+ lymphocytes develop within the dysplastic thymus; although lymphocytes have not been seen in nude thymus^{3,4}, serial sectioning of foetal or newborn glands will be required to exclude this possibility.

These results suggest that most, if not all, nude mice have significant numbers of T cells. Until it is known whether these cells are immunologically competent, it would be wise to interpret experiments involving these mutants with caution.

I thank Dr G. M. Iverson for supplying the anti- θ C₃H serum, Drs I. Lefkowitz and L. La Fleur for providing nude mice and Dr J. J. T. Owen for helpful discussion.

Note added in proof. Since submitting this manuscript, it has been brought to my attention that Vassalli and colleagues²³ found that 1% of cells in nude spleen labelled in an indirect immunofluorescence assay with a heterologous anti-T cell antiserum (anti-MSLA). In addition, they found a small number of cells with an ultrastructural morphology which they considered to be characteristic of T lymphocytes.

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T Cells in Recognition of Histocompatibility Antigens

THE capacity of lymphoid cells from normal mice to recognise foreign histocompatibility antigens, as shown in the PAR test, might offer a further assay for the function of T cell receptors, if it could be shown that recognition depends on T cells rather than on B cells. (PAR is a product of antigenic recognition elaborated in one-way mixed lymphoid cell cultures.)

Technical details on test conditions and on PAR determinations have been described^{1,2}. The test provides a quantitative measurement of the recognition of alloantigens, present on F₁ hybrid target cells, by lymphoid cells of parental lineage. Interaction with antigen occurs *in vitro* within a few hours, but demonstration of the recognition product has to be done *in vivo* and seems to need the magnifying effect of a granulotactic mediator, possibly an antibody-antigen complex. The technical disadvantages of the test system are heavily outweighed by its extreme sensitivity³. A major drawback has been, however, that the cell type responding to histocompatibility antigens has been poorly defined. Using cells from various lymphoid organs of normal mice, I here report studies on the critical role of T and B cells in the formation of PAR.

CBA lymphoid cells or spleen cells from Balb/c or from nude (nu/nu) mice (backcrossed for seven generations to Balb/c) were used as aggressors (10^6 cells) and confronted *in vitro* with C57Bl/6 antigens present on 10^6 (C57Bl/6 $\times$ CBA)F₁ or (Balb/c $\times$ C57Bl/6)F₁ target spleen cells, respectively. Culture supernatants were collected after various intervals and tested for PAR by injection into the skins of hamsters and determination of the number of accumulated polymorphonuclear cells found 24 h later in trypsinised skin reactions. Only intervals resulting in peak responses are shown. Activation of thymus cells used as thoracic duct lymphocytes (T.TDL) was as described⁴ (see also Table 1). Activated thymus cells (ATC) recovered from spleens (Table 1) and the treatment of cells with anti- θ C₃H and complement (1:10) were also as described⁵ (see also Table 1). Sensitised spleen cells (CBA anti-C57Bl/6) were obtained from CBA mice 21 d after full-thickness C57Bl/6 skin grafts.

Results on PAR assays are shown in Table 1. Balb/c spleen cells reacted to C57Bl/6 antigens maximally within 4 h at 37° C, but spleen cells from nude mice failed to

Table 1 Capacity of Various Lymphoid Cells to Recognise Alien Transplantation Antigens (PAR Assay)

Aggressor cells from	Recognition system	Target spleen cells	Peak response (h at 37° C)	PAR ± s.e. * at peak response
Balb/c spleen } nu/nu spleen }		(Balb/c × C57Bl/6)F ₁	4 (None after 2, 4, 7)	10.01 ± 0.08 0
CBA spleen	}	(C57Bl/6 × CBA)F ₁	7	8.41 ± 0.33
CBA bone marrow			7	2.31 ± 0.12
CBA TDL			7	7.69 ± 0.29
CBA anti-C57Bl/6 spleen			1	16.39 ± 1.25
CBA native thymus			(None after 1, 4, 7, 10)	0
CBA ATC (spleen) †			7	7.83 ± 0.58
CBA ATC (spleen) ‡			7	9.06 ± 0.84
CBA ATC (T.TDL) §			1	12.15 ± 0.46
CBA spleen + anti-θC3H 1:8 to 1:32 + C'			(None after 7)	0
CBA bone marrow + anti-θC3H 1:10 + C'			(None after 1, 2, 4, 7, 10)	0

* Number of PMN cells per skin site. Values corrected for syngeneic controls¹.

† Activated thymus cells. Activation: 10⁷ thymus cells (5- to 6-week-old CBA) injected intraperitoneally into 850 r (C57Bl/6 × CBA)F₁ mice. Spleens collected 5 d later⁵.

‡ Activated thymus cells. Activation according to and by ref. 4, but used as day 5 spleen cells.

§ Activated thymus cells. Activation*: 10⁸ thymus cells (5- to 6-week-old CBA) injected intravenously and 10⁸ thymus cells injected intraperitoneally into 750 r (C57Bl/6 × CBA)F₁ mice. Cannulation of thoracic duct on day 4 and for 24 h.

react, presumably because of a lack of T cells⁶⁻⁸. Taking the response of spleen cells in the recognition system CBA to C57Bl/6 as standard, recognition of CBA thoracic duct small lymphocytes (TDL) was very similar and contrasted well with CBA bone marrow cells, known to contain only few T cells^{9,10}, and from native thymus cells which seem to contain either extremely few antigen-sensitive T cells or only precursors of such cells. In sharp contrast to the response of native thymus cells, ATC reacted well. Differences were observed, however, depending on whether ATC were collected from thoracic duct or from spleen. The former (T.TDL) displayed a response characteristic of sensitised cells (CBA anti-C57Bl/6 spleen cells) with peak formation of PAR and with large amounts after cultivation for only 1 h (ref. 11). ATC collected from spleen behaved like normal spleen cells and both activation procedures^{4,5} gave identical results. The different behaviour of ATC seems to indicate that the cells follow distinct pathways in irradiated F₁ hosts. Cells differentiated to normal competence (or possibly returned to it after passing through an effector stage) settle in the spleen; cells differentiated to killer lymphocytes circulate and can be collected from the thoracic duct. Corroborating these results are those on cell suspensions in which T cells have been eliminated by treatment with anti-θ C3H serum and complement. B cells from spleen or from bone marrow were incapable of PAR formation.

Together with previous work^{1,2,5}, my results indicate that recognition of histocompatibility antigens by lymphoid cells as measured in the PAR assay is a T cell function. Antigenic response was lacking or reduced if aggressor cells contained no, or only few, T cells. The PAR assay failed to measure recognition of alloantigens by B cells. In line with other T cell functions, recognition of transplantation antigens is an extremely specific process^{3,8} and seems to be a prerequisite for manifestations of immunity¹² and tolerance¹³.

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Differences between Cytoplasmic Glucocorticoid-binding Proteins shown by Heterogeneity of Nuclear Acceptor Sites

It is now widely accepted that most, if not all, glucocorticoid responses in target tissue are mediated by specific steroid receptor molecules in the cytoplasm^{1,2}. Following association between steroid and receptor, there is transport of the steroid to the nucleus where subsequent interaction with the genome presumably alters transcriptional processes³. This scheme does not yet satisfactorily explain the widely differing responses of various tissues to glucocorticoids. Specificity of the kind of response observed could lie in differences in the receptor molecule itself and/or in the ability of a common receptor molecule to interact only with certain 'exposed' parts of the nuclear material in a given cell. Some evidence has favoured the latter interpretation⁴, but there has not yet been support for the former contention. In this report, we present evidence that at least some degree of specificity of response may be mediated by subtle differences in the cytoplasmic corticosteroid-binding proteins between tissues with differing kinds of responses to glucocorticoids. Our data further suggest that there are intranuclear binding sites for cytoplasmic glucocorticoid receptors which are of high affinity and saturability and which can distinguish between glucocorticoid receptors of differing origin.

In these studies, hepatoma tissue culture (HTC) cells and mouse fibroblasts (L cells) were grown in tissue culture and collected by standard methods^{5,6}. Both HTC⁷ and L cells⁸

have high affinity cytoplasmic receptor molecules and there is considerable evidence to implicate these proteins in the glucocorticoid response of both tissues. The responses themselves are dissimilar with specific increases in enzyme synthesis⁹ and in Phe-tRNA¹⁰ noted in HTC cells⁹ and a general inhibition of macromolecular synthesis in L cells¹¹. Neither of these cells' steroid binding molecules has been extensively characterised. As Fig. 1 shows, the binding affinities of the binding protein from HTC and L cells for the glucocorticoid dexamethasone are very similar. There does not seem to be significant interaction between cytoplasmic receptors from HTC and L cells because mixes of the two cytosols show essentially additive binding of glucocorticoid without obvious alteration in affinity.

Similarly, efforts to distinguish between HTC and L cell receptors by differences in heat inactivation showed small differences at 30° C (Fig. 2), and no differences at 34° C. Physicochemical characterisations of other glucocorticoid receptors have revealed, in general, close similarity¹².

To examine better the physiological properties of the cytoplasmic receptors from these two cell types we studied their uptake and binding to isolated nuclei in an *in vitro* system. Nuclear binding is a temperature-dependent process presumably involving a transformation in the cytoplasmic receptor. At 20° C we observed a depletion of cytoplasmic receptor in this *in vitro* system far greater than that due to heat inactivation and occurring coincidentally with the appearance of counts in the nuclei. Others have not found it necessary to warm the nuclei to obtain uptake of the temperature-transformed cytoplasmic receptors¹. Results at 0° C and 37° C are similar to those reported before¹³.

Nuclear binding of cytoplasmic receptor-steroid complex is of high affinity, and in our *in vitro* system shows saturability (Fig. 3). If it be assumed that one steroid molecule is bound per molecule of cytoplasmic receptor then the molar concentration of receptor in the incubation mix can be calculated. It can be seen that increases in homologous cytoplasmic receptor concentration above about 2.0 nM do not result in further increases in nuclear uptake of steroid. There is virtually no uptake of steroid by the nuclei in the absence of added cytoplasmic receptor. The values obtained for number of sites and affinity for HTC cells are similar to those reported before¹³. Both HTC and L cell nuclei have similar numbers of binding sites for their homologous receptor proteins on a per mg of protein basis. These sites may involve DNA, chromatin proteins or both. Work by others suggests that the nuclear sites for HTC cells may

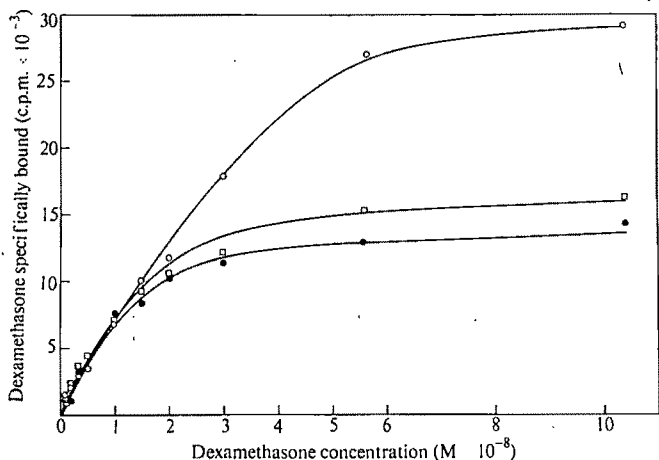


Fig. 1 Binding of ³H-dexamethasone (Amersham, 24 Ci mmol⁻¹ used throughout) to cytoplasmic receptors from HTC (●) and L cells (□); and to a mixture of HTC and L cell cytosols (○). Preparation of cell extracts and binding reactions were carried out using methods described previously¹². HTC⁹ and L cells⁶ were grown in suspension culture using published techniques.

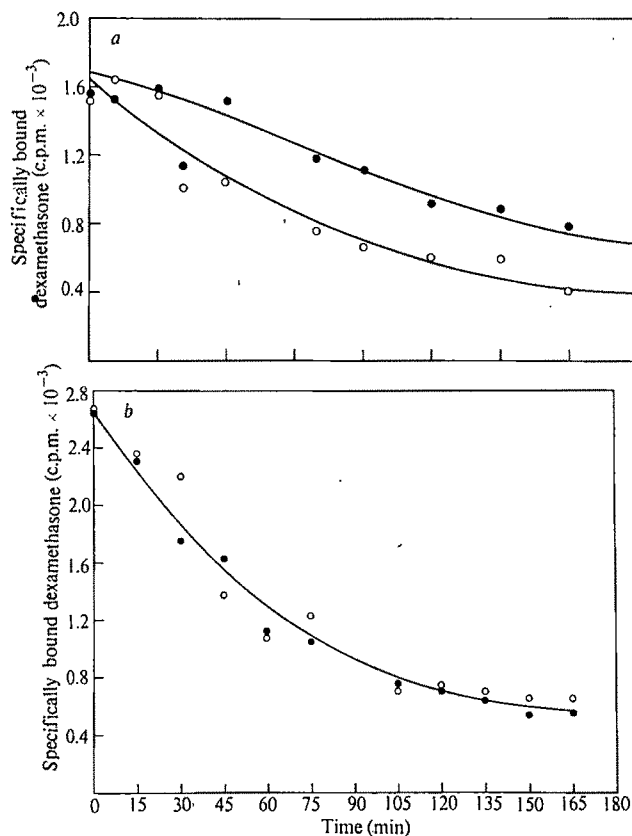


Fig. 2 *a*, Heat inactivation of HTC cell (●) and L cell (○) cytoplasmic receptors at 30° C. Paired samples of cytosol were equilibrated with 8×10^{-8} M ³H-dexamethasone in the presence or absence of 10^{-4} M unlabelled dexamethasone for 2.5 h at 0–2° C. At the start of the experiment the samples were placed in a 30° C water bath and aliquots removed in triplicate from both tubes at various times. Binding studies were performed using a modification of the DEAE-cellulose filter paper assay¹⁴ in which filters were initially washed with buffer I (20 mM Tris-HCl, pH 7.6, 1 mM MgCl₂; 2 mM CaCl₂; and 0.25 M sucrose) and the sample for assay run through the filter slowly after initial dilution in 15 volumes of buffer I. The filters were washed exhaustively with buffer I, air dried and counted in NCS (Amersham)-Liquifluor-toluene in a liquid scintillation counter (efficiency for ³H ~20%). Results were comparable to the charcoal assay techniques¹². Counts bound represent triplicate determinations of the difference between total counts bound and the non-competable background (usually less than 20% of the total counts on the filter). *b*, Heat inactivation of HTC (●) and L (○) cell cytoplasmic receptors at 34° C; methods were as described above.

consist of DNA¹³ although progesterone binding in other cell systems may require non-histone chromatin proteins and DNA⁴. Binding of label to nuclei in our *in vitro* system is felt to be specific in that there is an absolute requirement for the temperature-transformed cytoplasmic receptor and the system shows saturability at concentrations of cytoplasmic receptor which seem to be physiologically reasonable.

Since the phenotypic response of HTC and L cells to glucocorticoid is so different, and since biochemically the cytoplasmic receptors appear so similar, we were interested in knowing whether cytoplasmic steroid-receptor complex from one cell could interact with the nuclear sites of the other cell. If so, would there be competition between receptors from different sources for these nuclear sites? That is, once nuclear sites were saturated with homologous receptor protein were there additional sites which could be detected by cytoplasmic receptor from another source? Figure 4 shows that HTC cytoplasmic receptor complexes can bind to L cell nuclei to an approximately similar extent as homologous cytoplasmic receptor (*A*). Similarly, L cell cytoplasmic receptors can bind to HTC cell nuclei to an extent comparable

to that of HTC cell receptors (B). Furthermore, these heterologous systems show similar binding affinities and saturation phenomena characteristic of the homologous *in vitro* systems shown in Fig. 3.

Figure 3 shows that homologous nuclear saturation is maintained at a plateau level over a range of steroid-receptor complex concentrations. By saturating nuclei, it is possible to do mixing experiments in which additional steroid-cytoplasmic receptor from another cell is added to the incubation mix. In each experiment a saturation curve with the appropriate receptor complex was done as in Fig. 3 to show that the amount of the initial cytoplasmic receptor was saturating. Under these conditions, additional nuclear binding above plateau levels for the saturating receptor would be detected if the added heterologous receptor were occupying different sites. Interaction between cytoplasmic receptors was thought to be unlikely (see Fig. 1). As Fig. 4 shows, we found that when HTC cell nuclei were saturated with HTC cell receptor, they would bind glucocorticoid receptors from L cells. Conversely, when L cell nuclei were saturated with L cell cytoplasmic steroid binding complexes it was possible to detect additional sites which bound HTC cell receptors. Under our conditions, it was not possible to state whether or not there was any overlap between sites occupied by the two cytoplasmic receptors. Experiments involving sequential nuclear binding with saturating amounts of different receptor are currently under way.

These results suggest that HTC and L cells possess different cytoplasmic receptors which can be distinguished by their

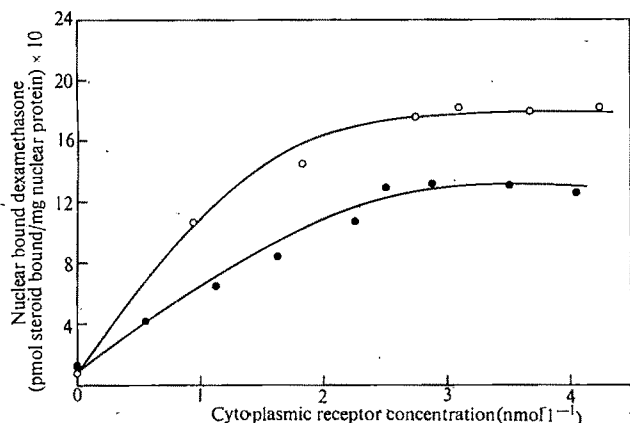


Fig. 3 Nuclear binding of HTC cell steroid receptor complexes by HTC cell nuclei and L cell steroid receptor by L cell nuclei. Cytosol was prepared¹² in buffer I and incubated for 2 h at 0–2° C with 8×10^{-8} M ^3H -dexamethasone in the presence or absence of 10^{-5} M unlabelled dexamethasone. Estimates of cytoplasmic receptor concentrations were obtained using the method described in Fig. 2. Nuclei were prepared by homogenising the cells in a tight fitting Dounce homogeniser in buffer I without sucrose and collecting the nuclear pellet by centrifugation at 800g for 5 min. This pellet was suspended and washed three times in buffer I and then incubated at 0–2° C for 2 h with 8×10^{-8} M ^3H -dexamethasone in the presence or absence of 10^{-5} M unlabelled dexamethasone to compete with the labelled steroid. After preliminary incubation of both nuclei and cytosol with steroid, they were mixed in a ratio of 1 : 4 (v/v), uncompeted cytosol with uncompeted nuclei and competed cytosol with competed nuclei. Before mixing, cytosol receptor was diluted with varying amounts of buffer I which had been pre-equilibrated with equivalent concentrations of radioactive or radioactive plus unlabelled steroid. After 75 min at 20° C, the nuclei were collected by centrifugation and washed three times in buffer I. The nuclei were sonicated in a small amount of water in a Bronwill sonicator (10 s, setting 15) and a Lowry protein determination¹⁵ was done on an aliquot. A further aliquot was counted in a liquid scintillation counter in 8 volumes NCS to which was added 10 ml of Liquifluor-toluene. In all cases, specifically bound nuclear steroid represents the difference between the total nucleus-bound counts and the counts bound in the competed sample containing unlabelled steroid as well as ^3H -dexamethasone. HTC cell cytosol plus HTC cell nuclei (○); L cell cytosol plus L cell nuclei (●).

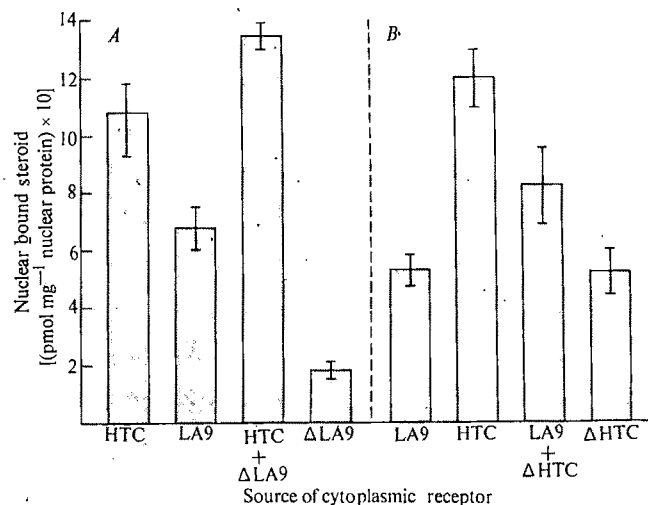


Fig. 4 A, Binding of various cytoplasmic receptors to HTC cell nuclei. These experiments were performed in a manner similar to those in Fig. 3. In each experiment a nuclear binding curve as shown in Fig. 3 was generated so that it would be clear that sufficient homologous receptor was present to saturate all nuclear sites to which it would bind. Then an additional amount of L cell cytoplasmic receptor was added to the incubation mix. After 75 min of incubation, nuclear binding was assayed as described in Fig. 2. ΔLA9 represents the increment in nuclear bound counts observed with the small amount of added L cell cytoplasmic receptor. B, Binding of various cytoplasmic receptors to L cell nuclei. Techniques similar to those described above were used except that L nuclei were mixed with saturating concentrations of HTC or L cell cytoplasmic receptor and an additional amount of HTC cell receptor was added to the incubation mix containing saturating amounts of L cell receptor. ΔHTC represents the increment in nuclear bound counts observed with the small amount of added HTC cell cytoplasmic receptor.

additive binding to nuclei. An implication is that nuclear binding can be used to assay for qualitative differences in corticosteroid receptors. It also seems that there must be different classes of sites in a given nucleus, able to recognise specific glucocorticoid receptors. It should be realised that the relationship of these nuclear sites, measured *in vitro*, to physiologically significant control sites is unknown. We cannot exclude the possibility that somehow receptor of one cell type facilitates entry of the other receptor, though this seems unlikely.

Previously, the presence or absence of steroid responsiveness has been attributed to the presence or absence of functional cytoplasmic receptor. Such data have not explained the qualitatively different tissue responses to the same hormone. Although the data here were obtained from mouse L cells and rat HTC cells, they nevertheless suggest that qualitative differences in cytosol receptors for glucocorticoids contribute to the specificity of phenotypic response in different tissues.

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Anticoagulant Action of Heparin

ANTITHROMBIN III (heparin cofactor) is known to inhibit thrombin¹ and Factor X_a¹⁻³ (activated Factor X). We have purified antithrombin⁴ from human plasma by a series of chromatographic and electrophoretic separation techniques. The homogeneity of the final product is demonstrated by disc gel electrophoresis, SDS gel electrophoresis and immuno-electrophoresis⁴. Using this preparation, we have shown that antithrombin forms a 1:1 stoichiometric complex with thrombin which cannot be dissociated with denaturing and reducing agents. Addition of heparin dramatically accelerates the rate of formation of this complex. Complex formation is completely dependent on an interaction between the serine active centre of thrombin and an arginine reactive site of antithrombin. Furthermore, ϵ -amino lysyl groups of antithrombin serve as binding sites for the highly negatively charged heparin. Based on these data and other evidence, we have proposed that heparin acts to accelerate inhibitor function by binding to antithrombin and inducing an allosteric modification in it, which renders the arginine in its reactive site more accessible to the serine in the active centre of thrombin⁴.

This mechanism suggested that all serine proteases within the coagulation cascade may be neutralised in a similar manner. To test this hypothesis we have examined the interaction of antithrombin and heparin with Factor XI_a (activated Factor XI), another serine protease⁵ generated during coagulation, whose physical properties and substrate specificity differ considerably from those of Factor X_a and thrombin.

Factor XI_a was purified from human plasma by DEAE-cellulose chromatography, celite adsorption-elution, hydroxyapatite chromatography, and polyacrylamide P-150 gel filtration according to the method of Amir *et al.*⁶ with minor modifications. The final product is free of coagulation Factors I, II, V, VII, VIII, IX and X as judged by fibrinogen determinations⁷ and one-stage assays using congenitally deficient plasmas as substrates⁸.

To ascertain whether antithrombin inactivates Factor XI_a, antithrombin was incubated with Factor XI_a at final concentrations of 64 units ml⁻¹ and 100 units ml⁻¹ respectively, and residual Factor XI_a activity was sequentially measured as a function of time. As shown in Fig. 1, there is a progressive decline in Factor XI_a activity. No significant reduction in this activity is, however, observed when buffer is substituted for antithrombin. When the neutralisation of Factor XI_a activity is plotted in semi-log fashion (not shown), the kinetics closely approximate those of a first order reaction.

To determine whether antithrombin is responsible for a significant proportion of the plasma's ability to inhibit Factor XI_a, we removed antithrombin from plasma by specific immunoprecipitation and measured the residual capacity of these samples to neutralise this activated intermediate. Plasmas deficient in C1 esterase inhibitor (C1INH) were employed in these experiments, since it is known to be responsible for 20% of the plasma's Factor XI_a inhibitory capacity¹⁹ and activation of the complement system during immunoprecipitation would result in its reduction. As shown in Table 1, specific immuno-

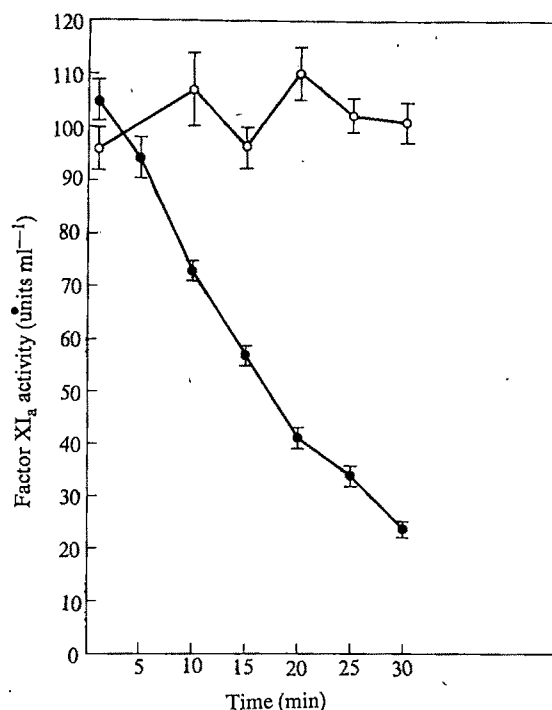


Fig. 1 Inhibition of Factor XI_a by antithrombin. Factor XI_a was incubated with buffer or antithrombin in albuminised plastic tubes at 37° C. 0.02 ml of Factor XI_a was added to either 0.38 ml of 0.15 M NaCl in 0.01 M Tris (pH 7.5) or 0.18 ml of this buffer and 0.2 ml antithrombin. The final concentrations of Factor XI_a and antithrombin used were 100 units ml⁻¹ (0.002 AU ml⁻¹) and 64 units ml⁻¹ (0.060 AU ml⁻¹), respectively. Mixtures were separately incubated for varying periods of time and assayed in triplicate for residual Factor XI_a. Each point represents the mean obtained for two separate incubation mixtures $\pm$ s.e.m. $\circ$ — $\circ$, Factor XI_a + buffer; $\bullet$ — $\bullet$, factor XI_a + antithrombin. Factor XI_a activity was measured by a modification of the method of Nossel²¹ utilising cephalin²² and plasmas congenitally deficient in this coagulation protein. The initial concentrations of Factor XI_a preparations were estimated by comparison with the Factor XI content of pooled plasma obtained from twenty-five normal subjects. Assays of Factor XI levels in plasma were performed by the method of Rapaport *et al.*²³ with the mean value of this plasma component arbitrarily set at 100 units ml⁻¹. Antithrombin (heparin cofactor) activity was determined by a modification of the method of Gerandas²⁴ in the absence of heparin or by the method of Abildgaard⁹ in the presence of heparin. Purified human thrombin²⁵, (3,200 NIH units mg⁻¹) was employed in both types of activity measurements. The concentration of antithrombin was also obtained by immunological assay using the technique of Laurell²⁶ with monospecific antisera prepared by immunizing rabbits with the purified protein. Activity and immunological measurements were in excellent agreement and were compared to a pool of twenty-five normal plasmas. Unless otherwise indicated, the concentrations of antithrombin cited represent an average of all types of determinations. The mean concentration of antithrombin was arbitrarily set at 100 units ml⁻¹.

precipitation of 71–80% of plasma antithrombin by a γ -globulin concentrate directed against this protein produces, in all cases, corresponding declines in the ability of these samples to inhibit Factor XI_a. In each instance, non-specific effects of γ -globulin addition have been accounted for by comparing these results with duplicate samples to which we have added a "bland" γ -globulin concentrate obtained from non-immunised rabbits. From these data we estimate that antithrombin is responsible for about 50% of these plasmas' capacity to neutralise Factor XI_a. Using the data of Ratnoff *et al.*¹⁰, on the relative importance of plasma C1INH as an antagonist of Factor XI_a, we suggest that antithrombin is responsible for about 40% of the Factor XI_a inhibitory capacity of normal plasma, with the residual 40% inhibitory capacity due perhaps to the inhibitor recently isolated by Amir *et al.*¹¹.

These three plasma protease inhibitors only slowly neutralise Factor XI_a activity. If the antithrombin-Factor XI_a interaction

were to be dramatically accelerated by heparin, then the addition of this anticoagulant to plasma would transform antithrombin from a plasma inhibitor of some importance to the primary antagonist of Factor XI_a action. To test this possibility we examined the time-dependent decay of Factor XI_a in the presence of antithrombin and heparin.

Methodological problems make such measurements difficult. Heparin is known to inhibit (through antithrombin) the action of Factor X_a on prothrombin¹⁻² as well as that of thrombin on fibrinogen¹, and a valid determination of the proteolytic activity of Factor XI_a depends on the degree to which this species triggers these terminal reactions of the coagulation cascade. Therefore heparin as well as antithrombin-heparin complexes must be removed from incubation mixtures before assaying them for Factor XI_a. Well-recognised approaches to inhibiting heparin's action such as protamine and heparinase were initially examined. Protamine was found not only to inhibit heparin but also to reduce directly the activity of Factor XI_a. Heparinase at concentrations of 0.13 mg of crude enzyme ml⁻¹ (ref. 12) was shown to rapidly destroy free heparin but only slowly affect heparin bound to antithrombin. The addition of 9 mg of DEAE-cellulose to test incubations, centrifugation of these mixtures and use of the supernatants, proved, however, to be a rapid means of selectively eliminating free or bound heparin without altering the level of Factor XI_a.

Several experiments demonstrated the validity of this approach: First, when heparin and Factor XI_a were incubated together and processed in the above fashion, no significant decrease in Factor XI_a activity was detected (Fig. 2). Second, when antithrombin and heparin were incubated together for 5 min, the mixtures treated with DEAE-cellulose, and the resulting supernatants incubated with Factor XI_a, only a minimal reduction in Factor XI_a activity was seen (Fig. 2). Third, when Factor XI_a was incubated with buffer and treated with DEAE-cellulose, the supernatants obtained showed no significant reduction in the initial Factor XI_a activity (Fig. 2).

To test whether heparin accelerates the interaction between Factor XI_a and antithrombin, mixtures of antithrombin, heparin, and Factor XI_a at final concentrations of 36 units

ml⁻¹, 0.7 units ml⁻¹, and 100 units ml⁻¹, respectively, were incubated together for 1, 3, or 5 min before the addition of DEAE-cellulose. After centrifugation, the respective supernatants were analysed and Factor XI_a activity was found to be virtually absent in all incubation mixtures (Fig. 2). In other experiments (not shown), shorter periods of incubation (0.1 to 0.5 min) revealed the same degree of Factor XI_a inhibition. These results are to be compared with those obtained when the inactivation was examined in identical conditions, but with the omission of heparin. In these mixtures only a minimal time-dependent reduction in Factor XI_a activity was observed (Fig. 2). Therefore heparin dramatically accelerates the formation of a Factor XI_a-antithrombin complex. On the basis of the neutralisation of Factor XI_a by antithrombin in the absence of heparin, as well as our knowledge of the mechanism of inhibitor action, we may confidently presume that inactivation of Factor XI_a follows this interaction.

Thus Factor XI_a, like Factor X_a and thrombin, is a serine protease which is slowly but progressively inhibited by antithrombin in the absence of heparin and virtually instantaneously neutralised by antithrombin in the presence of this anticoagulant. On the basis of these data and the known mechanism of action of antithrombin⁴, we predict that antithrombin will be shown to inactivate the other remaining serine proteases of the coagulation cascade, Factor VII_a (ref. 13), Factor IX_a (ref. 14) and Factor XII_a (ref. 15), and that heparin will accelerate each of these interactions. Indeed, Aronson, using antithrombin prepared by us, has already confirmed this hypothesis for Factor IX_a (personal communication).

Furthermore this linkage of the anticoagulant action of heparin to the early "contact phase" of the coagulation cascade suggests that antithrombin may play a significant role in maintaining nonthrombogenic properties of artificial as well as natural surfaces. When heparin is covalently bonded to a variety of materials, they prove to be highly thromboresistant^{16,17}. It is probable that they owe this property to "activated" antithrombin, bound at the blood-surface interface, which can rapidly neutralise serine proteases generated during the initial contact phase of clotting and thus abort

Table 1 The Factor XI_a Inhibitory Activity in C1INH-deficient Plasmas Depleted of Antithrombin

Sample	Initial antithrombin concentration (units ml ⁻¹)	Initial C1INH concentration (units ml ⁻¹)	% Antithrombin-heparin cofactor activity removed by immunoprecipitation	Factor XI _a removed after 15 min of incubation at 37° C (units ml ⁻¹)
Buffer	—	—	—	7
C1INH-deficient plasma 1	100	8.7	—	—
a + γ-globulin concentrate directed against antithrombin	—	—	80	56
b + "bland" γ-globulin concentrate	—	—	0	75
C1INH-deficient plasma 2	100	12.0	—	—
a + γ-globulin concentrate directed against antithrombin	—	—	71	39
b + "bland" γ-globulin concentrate	—	—	0	73
C1INH-deficient plasma 3	110	19.0	—	—
a + γ-globulin concentrate directed against antithrombin	—	—	76	55
b + "bland" γ-globulin concentrate	—	—	0	70

Plasmas deficient in C1INH were obtained from three patients with hereditary angioneurotic oedema using two-syringe technique, plastic vessels and sodium citrate as anticoagulant (0.38% final concentration). They were individually assayed for antithrombin (see legend to Fig. 1) and C1INH by the technique of Laurell with monospecific sera (normal range: 44–177 units ml⁻¹). Samples were then stored at –70° C. Sera were obtained from rabbits immunised with purified antithrombin as well as rabbits which had not been immunised. The γ-globulin fractions were prepared by the method of Stanworth²⁷, concentrated to 100 AU ml⁻¹, dialysed against 0.15 M NaCl in 0.01 M Tris (pH 7.5) and heated to 60° C for 1 h. These γ-globulin concentrates did not inhibit Factor XI_a nor did they exhibit antithrombin or heparin cofactor activity. Monospecificity of the γ-globulin concentrate directed against antithrombin was demonstrated by immunoelectrophoresis and Ouchterlony double diffusion. C1INH deficient plasmas (0.3 ml) were added to both types of γ-globulin concentrates (0.9 ml) and the mixtures were incubated for 30 min at 37° C and 90 min at 4° C. The samples were centrifuged at 15,000g and 4° C for 20 min. The resulting supernatants were assayed for residual heparin cofactor activity (measurement of antithrombin activity in the presence of heparin, see legend to Fig. 1). In addition, residual Factor XI_a inhibitory activity was determined by adding 0.2 ml of supernatant to 0.18 ml of 0.15 M NaCl in 0.01 M Tris (pH 7.5) and 0.02 ml of Factor XI_a (final concentration of 100 units ml⁻¹). After 15 min of incubation at 37° C, the mixtures were assayed in triplicate for Factor XI_a activity (see legend to Fig. 1). Controls were obtained for the same period of incubation by replacing the supernatants with 0.15 M NaCl in 0.01 M Tris (pH 7.5). Figures given represent the means obtained for duplicate incubation mixtures prepared on two separate days. The relative Factor XI_a inhibitory capacity of plasmas (not given) was estimated by a plot of plasma dilution against the log of the residual Factor XI_a activity at 15 min.

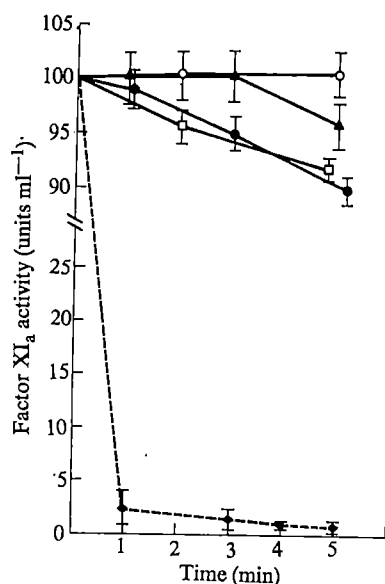


Fig. 2 Inhibition of Factor XI_a by antithrombin and heparin. Two distinct sequences of addition of Factor XI_a to other components were employed to obtain the above data. The first incubation sequence used duplicate samples of 1.6 ml composed of Factor XI_a added to either buffer, heparin, antithrombin or antithrombin and heparin. In this instance, Factor XI_a was employed at a final concentration of 100 units ml⁻¹ while heparin and antithrombin, if present, were used at final concentrations of 0.7 units ml⁻¹ and 36 units ml⁻¹, respectively. All samples were incubated for 1–5 min at 37° C, dried DEAE-cellulose (9 mg) was added with gentle agitation, the mixtures were immediately centrifuged at 15,000g for 30 s and the resulting supernatants were assayed in triplicate for residual Factor XI_a activity. The second incubation sequence used duplicate samples of 1.2 ml consisting of antithrombin and heparin at final concentrations of 48 units ml⁻¹ and 0.93 units ml⁻¹, respectively. Both samples were incubated at 37° C for 5 min, dried DEAE-cellulose (9 mg) was added with gentle agitation, the mixtures were centrifuged at 15,000g for 30 s and the resulting supernatants were obtained. Factor XI_a was added to these supernatants in a 1 : 3 (v/v) ratio such that its final concentration was 100 units ml⁻¹; the samples were incubated at 37° C for 2–5 min, and the residual Factor XI_a activities were determined in triplicate. Values given represent the mean Factor XI_a activity $\pm$ s.e.m. In all cases, components have been either dialysed against or extensively diluted in buffer (0.15 M NaCl in 0.01 M Tris, pH 7.5). $\circ$ — $\circ$, Factor XI_a + buffer; $\triangle$ — $\triangle$, factor XI_a + heparin; $\square$ — $\square$, factor XI_a + heparin-antithrombin-treated supernatant; $\bullet$ — $\bullet$, factor XI_a + antithrombin; $\blacklozenge$ — $\blacklozenge$, factor XI_a + heparin + antithrombin.

the production of the terminal serine proteases responsible for thrombin formation. By analogy, since heparin has been isolated from vessel walls^{18,19}, as well as other organs²⁰, it may prove fruitful to reinvestigate vascular endothelial thromboresistance in terms of heparin or heparin-like material bound to surfaces. The presence of such substances coupled with the unique properties of antithrombin suggests that this inhibitor is the critical barrier against activated coagulation factors at the vessel wall interface and thus provides a crucial link between surface properties and the coagulability of blood.

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Perception of Polarised Light in Insects by Filter Mechanism

THE response of a single visual cell of an insect, intracellularly recorded¹⁻³, to polarised light (PL) is relatively small but, as is generally known, insects display a great capability of orientating to polarised light. Here I suggest that this contradiction can be explained with the aid of a filter mechanism.

My theory is based on some well known facts. Many insects have so-called tiered retinulas with one or more basal (or proximal) visual cells and both theoretical⁴ and experimental^{5,6} results indicate that the microvilli of rhabdomeres exhibit dichroism with a dichroic ratio of 2. Furthermore, the longer the dichroic rhabdomere, the lesser its dichroic ratio, which is 1 in the limit because of 100% absorption for any orientation of the E vector. Thus, a long rhabdomere could hardly act as a PL detector in the eye of an insect.

The principal idea presented here is that a distal rhabdomere serves as a PL filter (analyser) for linearly polarised light from blue sky, whereas the proximal one absorbs or measures the intensity of PL transmitted by the distal rhabdomere (Fig. 1).

Let the intensity of incident PL be I_0 . When the E vector of PL is parallel to the long axes of the microvilli, ~~this is~~, when it is orientated in the x direction, the intensity of light transmitted by the distal rhabdomere and entering the proximal rhabdomere will be $I_{xd} = I_0 \exp(-x_d) = I_0 \exp(-k l_d)$ where k is the absorption coefficient and l_d is the length of the distal rhabdomere. In turn, $k = 2.3 \epsilon c_x$ where ϵ is the molar extinction coefficient, c_x is the concentration of photopigment molecules orientated in the x direction, and 2.3 is the constant derived from changing from the generally used extinction coefficient $K = \epsilon c_x$ to the absorption coefficient (k) used here; that is

$$I_{xd} = I_0 \exp(-2.3 \epsilon c_x l_d) = I_0 \times 10^{-\epsilon c_x l_d}$$

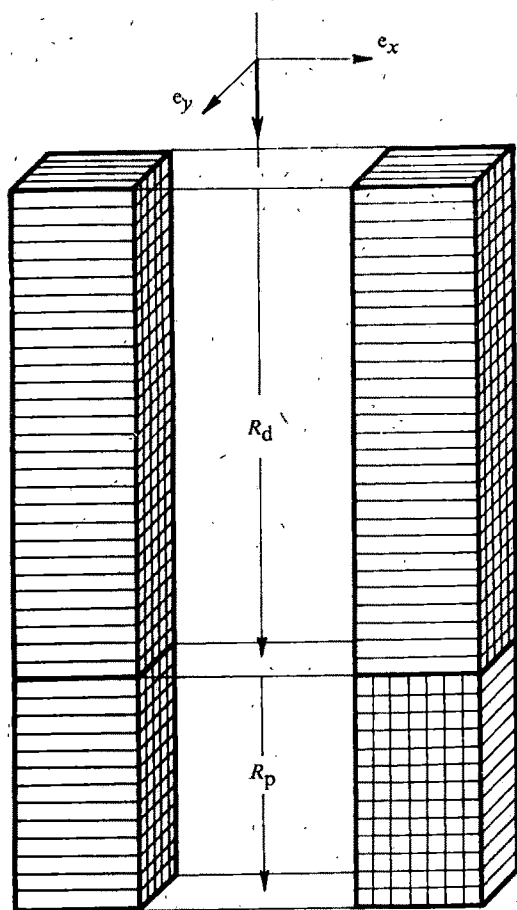


Fig. 1 The distal (R_d) and the proximal (R_p) rhabdomeres with parallel (left) or perpendicular (right) microvilli. Light propagates as indicated by thick arrow, thin arrows show the x - and y -orientations of the E vector.

On rotation of the E vector at an angle of 90° (y direction), transmitted light intensity will be given by $I_{y_d} = I_0 \exp(-y_d)$ where $y_d = 2.3 \epsilon c_y l_d$, with c_y concentration of photopigment molecules orientated in the y direction, and $D = c_x/c_y$ is the dichroic ratio of a microvillus. The ratio of transmissions is

$$r_{td} = I_{y_d}/I_{x_d} = \exp(-y_d)/\exp(-x_d) \quad (1)$$

whereas the relation between absorptions which defines the PL response of the distal cell is

$$r_{ad} = [1 - \exp(-x_d)]/[1 - \exp(-y_d)] \quad (2)$$

As the same is true for the proximal rhabdomere, with $x_p = 2.3 \epsilon c_x l_p$ and $y_p = 2.3 \epsilon c_y l_p$ the relation between absorptions can be found for the proximal rhabdomere which, as suggested by this model, is responsible for the strong PL response of the whole compound eye.

$$r_{ap||} = I_{y_p}/I_{x_p} = [\exp(-y_d)/\exp(-x_d)][(1 - \exp(-y_p))/(1 - \exp(-x_p))] \quad (3)$$

if the microvilli of both the rhabdomeres are parallel, and

$$r_{ap\perp} = [\exp(-y_d)/\exp(-x_d)][(1 - \exp(-x_p))/(1 - \exp(-y_p))] \quad (4)$$

if the mutual orientation of the microvilli is perpendicular, since for the proximal rhabdomere $c_{x\perp} = c_{y||}$ and $c_{y\perp} = c_{x||}$.

Let the dichroic ratio $D = c_x/c_y$ of a single microvillus equal 2, as has been mentioned above, and the absorption coefficient be $1.7\% \mu\text{m}^{-1}$ as in crabs⁵ (that is a specific absorptivity of 0.017) when the E vector is parallel to the microvilli and $0.85\% \mu\text{m}^{-1}$ (or a specific absorptivity of 0.0085) for the perpendicular orientation of the E vector. For a distal rhabdomere 200 μm in length, $x_d = (0.017 \times 200) = 3.4$ and $y_d = 1.7$. For the proximal rhabdomere, which is usually shorter (say 70 μm , near the

'optimal' value¹¹), $x_p = (0.017 \times 70) = 1.2$ and $y_p = 0.6$. Substituting these values in equations (2), (3) and (4), $r_{ad} = 1.18$ ('PL response' of the distal visual cell), $r_{ap||} = 3.5$ and $r_{ap\perp} = 8.5$ ('PL response' of the proximal, or basal, visual cell). Of course, using these figures it should be remembered that the real electrical response of the cell is approximately proportional to the log of intensity absorbed.

Thus, a basal cell may seem responsible for acute PL perception in insects although its rhabdomere, as well as those of other visual cells, is built from relatively unsuitable material, that is microvilli having a dichroic ratio as small as 2.

The chief consequence of this consideration is that information on PL must be processed in a differential way. As the relation between the absorption of the distal and the proximal rhabdomeres does not depend on intensity I_0 (if bleaching is small), both the cells can make inputs of opposite polarities to the higher neurones which may be defined as a PL detector and which does not seem to show appreciable response to changes in intensity I_0 . On rotation of the E vector, however, the output signal of the distal cell remains nearly constant ($r_{ad} = 1.18$ in the above example) although the signal of the proximal receptor is greatly modulated by this rotation and this results, in turn, in a drastic change in the relation a_d/a_p between absorptions in distal and proximal rhabdomeres.

Two long axons coming off cells 7 and 8 in the fly retina bypass the intermediate retina and end in the medulla⁷. Such an organisation of nerve connections may be taken as morphological evidence in favour of the above differential mechanism. Unfortunately, nothing is known about the nerve connections of basal cells in the honeybee eye. It may be of interest that such a mechanism can provide a strong PL response by the eighth visual cell in the fly retina where the microvilli of cells 7 and 8 are perpendicular, maximal response being for the E vector perpendicular to the microvilli of cell 7. According to my morphological data⁸, in the honeybee retina the ninth cell has to show a smaller response to PL than the eighth cell of the fly because of the parallel orientation of the microvilli of the ninth cell relative to the microvilli of 'filter' rhabdomeres.

It follows from the model presented here that the ninth cell in the bee retina must be the only visual cell showing strong PL response. This prediction is in excellent agreement with recent findings⁹. The mechanism suggested is not at variance with the dielectric waveguide theory¹⁰ which, although complicated enough, must be developed for the rectangular dielectric waveguide⁸. More details on the 'filter mechanism' are given elsewhere¹¹. A deep theoretical analysis of the PL sensitivity of the insect visual cell has recently been carried out by Snyder¹².

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Alteration of Visual Cortex from Environmental Asymmetries

Wiesel and Hubel have shown that if normal simultaneous binocular vision is prevented during a period when an animal is particularly sensitive to the nature of its visual input, substantial changes can occur in the visual system¹⁻³. A dramatic extension of the influence of visual deprivation was made a few years ago. Kittens were reared viewing contours of a given orientation, and physiological studies showed that their visual cortical neurones had become tuned to the orientation they had experienced^{4,5}. In a related study, kittens were raised with prisms that caused vertical disparities between the images of the two eyes. Later it was found that the distribution of optimal disparities for which binocular cortical neurones were most responsive had undergone a shift, apparently to compensate for the rearing condition⁶. There is now an indication that the modifications can occur from an exceedingly brief selective exposure^{7,8} and recent behavioural data complement the original physiological finding⁹.

Experimental results with certain human subjects point to an analogous bias in early visual environment with subsequent neural consequences¹⁰⁻¹². The bias is introduced through ocular astigmatism, a condition in which the refractive power of the eye varies meridionally such that maximum and minimum powers are orthogonal. The effect is that detail of a particular orientation may be in focus while features of other orientations are blurred. So, a condition of preferential visual exposure obtains, but the astigmatic condition imposes a subtle, rather than an all or none, bias.

To see if partially selective visual exposure is sufficient to modify cortical neurones, we reared kittens with artificially induced astigmatism and then studied them physiologically. We found that the visual cortex of these animals was, in fact, decidedly abnormal. Cells in the cortex favoured the orientation which was in focus during rearing.

Our kittens were kept in a fully darkened room until they were 4 weeks old. For 3 h daily during the next 25 d, they wore masks containing cylindrical ophthalmic lenses. The remainder of their time was spent in the dark. The masks were positioned in total darkness so that the kittens' sole visual experience was obtained through the lenses. Two groups of kittens were studied. The first included a control animal whose mask contained lenses with no refractive power. Three other animals wore cylindrical lenses which limited clear focus to vertical, horizontal, and oblique contours, respectively. As the kittens were allowed to roam freely, they received a considerable amount of close-up visual input where the effect of the lenses was reduced. A more severe bias was arranged for the second group of kittens. Their lenses were of higher refractive power and their exposure period was spent on a clear Lucite platform so that the bulk of their visual input was from relatively distant areas where the lenses cause maximum asymmetries.

At the conclusion of the rearing period, the kittens were examined electrophysiologically. Fluothane was used for the initial anaesthesia. After tracheal and intravenous cannulation, anaesthesia was maintained with a nitrous oxide mixture. Standard procedures were employed to preserve good optics and to minimise eye movements. With tungsten-in-glass microelectrodes, we recorded extracellularly from single neurones in the primary visual cortex. The various stimulus parameters relevant to the cells' activities were explored with stimuli presented by an overhead projector and receptive fields were plotted. By use of an X-Y recorder, stimuli were presented manually and by computer commands. Altogether, we studied 408 units in six animals.

Cortical cells in the normal cat usually respond very specifically to stimulus orientation and our rearing conditions make orientation the feature of key interest. Results for the first group of kittens are shown in Fig. 1. Each histogram

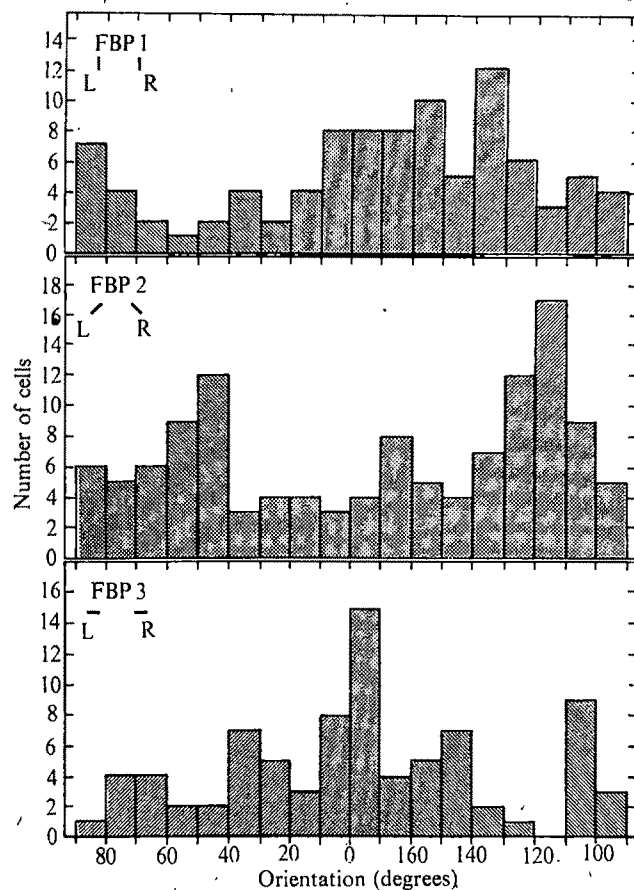


Fig. 1 Histograms showing the number of cells which respond best to a stimulus orientation within the 10° ranges indicated for three kittens. Each of the kittens has been reared with simulated astigmatism and the orientation which was in clear focus during rearing is indicated by the lines above the left (L) and right (R) eyes. Horizontal is 0° and vertical is 90°.

gives the total number of cells, both monocularly and binocularly driven, whose optimal stimulus orientation falls within a 10° range. 0° is horizontal and 90° is vertical. The insets indicate for each kitten the orientations which had been in clear focus during rearing. If the rearing conditions had influenced cortical neurones, the distribution of preferred orientations should peak at the clearly focused meridians. As shown in Fig. 1 the prediction holds for kittens FBP 2 and 3. For FBP 1, there is no skewing, but there is a substantial reduction in the number of binocularly driven cells as in the other astigmatic kittens (see below).

Figure 2 contains the results for the second group of kittens whose visual exposure was more strongly limited than the first group. Polar coordinates are used so that each line represents a cell whose preferred stimulus orientation is indicated by the angle of the line. For the normal cat, shown at the top, the distribution of preferred orientations is rather uniform and nearly all angles are represented. A marked departure from the normal pattern is seen in the astigmatically reared kitten. FBP 5, reared with oblique cylindrical lenses, received clear images of features with the indicated orientations. For each eye, the distribution of optimal orientations is clustered around the meridian which was in best focus during rearing, and the effect is most prominent in the left eye. A similarly asymmetrical orientation distribution is seen for FBP 6, and again a high density of preferred orientations occurs around the focused meridian, which in this case is horizontal. It is interesting to note that the right eyes of FBP 5 and FBP 6 show units for which the preferred orientations are nearly orthogonal to the meridian of clear focus. The factors most likely to be involved in this finding include accommodation and orientation

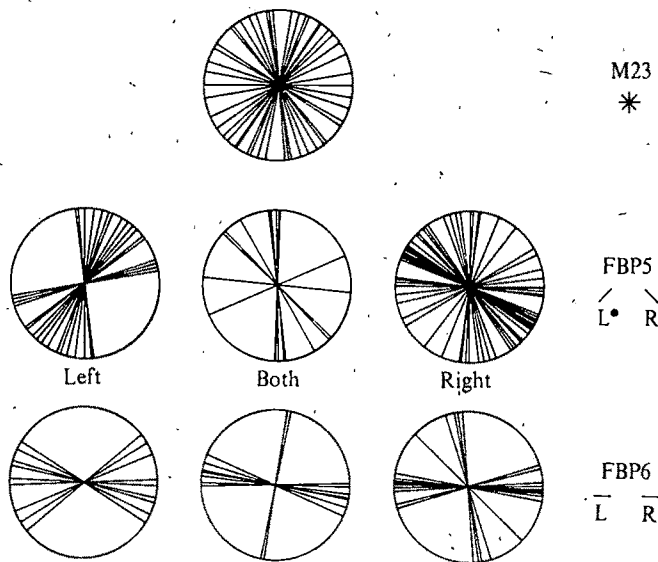


Fig. 2 Polar plots of preferred orientations for cortical cells are shown. Each line represents the optimal stimulus orientation for a single cell. The cat shown at the top is normal and below its name (M 23) several lines indicate that all orientations were present during rearing. The other cats have had a biased environmental upbringing caused by ocular astigmatism. As in Fig. 1, the lines above left (L) and right (R) eyes indicate the orientation which was in clear focus during rearing.

selectivity, as discussed in a detailed account of this work (Freeman and Pettigrew, unpublished).

Another finding, shown in Fig. 2, is the small number of units in the astigmatic kittens that are driven by both eyes. Only 25–35% of the cells are binocular as opposed to around 85% in the normal cat. One would expect a loss of binocularity in the case of oblique cylinders with different axes in front of each eye, but a reduction in the number of binocular cells also occurred with the bilaterally symmetrical biased kittens. The most likely explanation for the preponderance of monocular units is that the lenses were somewhat de-centred during rearing. Even a slight misalignment between the pupils and geometrical centres of the lenses would lead to considerable prismatic displacement.

The astigmatic rearing conditions also affected the limits of orientation selectivity. For normal cortical cells, stimulus orientation is usually very important, but the range over which the cell responds can vary considerably. Some cells are active over an angular region of only a few degrees while others respond over very wide ranges. In the astigmatic kittens, cells whose optimal orientation fell near the meridian of clear focus were also responsive over narrow to wide angular ranges as in normal kittens. But for the less frequently encountered units whose activity was highest when stimuli were presented away from the experienced meridian, we found that the response limits became broader. At a large angular distance from the clearly focused meridian, there were no finely tuned units. The implication is that a deficiency of features of a given orientation during early visual experience results in both a reduced number and a diminished selectivity of neurones which respond to that orientation.

Our results demonstrate that a subtle bias in the visual environment of a developing kitten is sufficient to markedly alter cortical physiology. The effects are graded in that our moderately biased kittens are modified less than the group for which bias was more severe. Thus, it appears that a kitten who has no previous visual experience is extremely sensitive to an environmental nuance. Even a relatively minor variation from normal exerts an influence on cortical connectivity.

It should, however, be mentioned that the type of approach

used in this investigation may be very useful in studying the physiological correlates of ocular refractive error.

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Perception of Random Dot Interference Patterns

THE observation that circular patterns are immediately perceived if a random dot pattern (Fig. 1a) is superimposed on itself and rotated slightly (Fig. 2a) indicates that the visual system detects local autocorrelations and integrates these to form a global circular percept¹. By varying both the local and global parameters describing the interference patterns, the functional organisation of the visual system can be probed and new perceptual effects discovered.

There is nothing special about the circular morphology of the random dot interference patterns. By performing other transformations of the random pattern about a fixed centre point before superposition new morphologies arise. For example, by uniformly expanding Fig. 1a, we obtain Fig. 1b. A starlike pattern is produced when Figs 1a and 1b are superimposed (Fig. 2b). If they are superimposed in a rotated position, spirals will result (Fig. 2c). If Fig. 1a is expanded in one direction and contracted in the orthogonal direction (Fig. 1c) a hyperbolic pattern will result after they are superimposed (Fig. 2d). In these cases, for each point, $P_i(x_i, y_i)$, in the initial pattern, the transformations generate a new point, $P'_i(x_i, y_i)$, given by

$$\begin{aligned}x'_i &= ax_i \cos \theta - by_i \sin \theta \\y'_i &= ax_i \sin \theta + by_i \cos \theta\end{aligned}\quad (1)$$

where the x coordinate is multiplied by a , the y coordinate is multiplied by b , and the pattern is rotated through an angle of θ . Since this finite transformation can be thought of as an iteration of an infinitesimal transformation, each pair of correlated points can be thought of as lying on a single trajectory in a phase plane representation of two coupled, autonomous linear differential equations corresponding to the infinitesimal transformation. The dot patterns have the same morphologies as the trajectories of this underlying differential equation and can be predicted using the qualitative theory of differential equations². The eigenvalues, $\Gamma_{\pm}$, of the linear transformation of equation (1)

$$\Gamma_{\pm} = [(a+b) \cos \theta \pm ((a-b)^2 - (a+b)^2 \sin^2 \theta)^{1/2}] / 2 \quad (2)$$

are related to the eigenvalues of the underlying differential

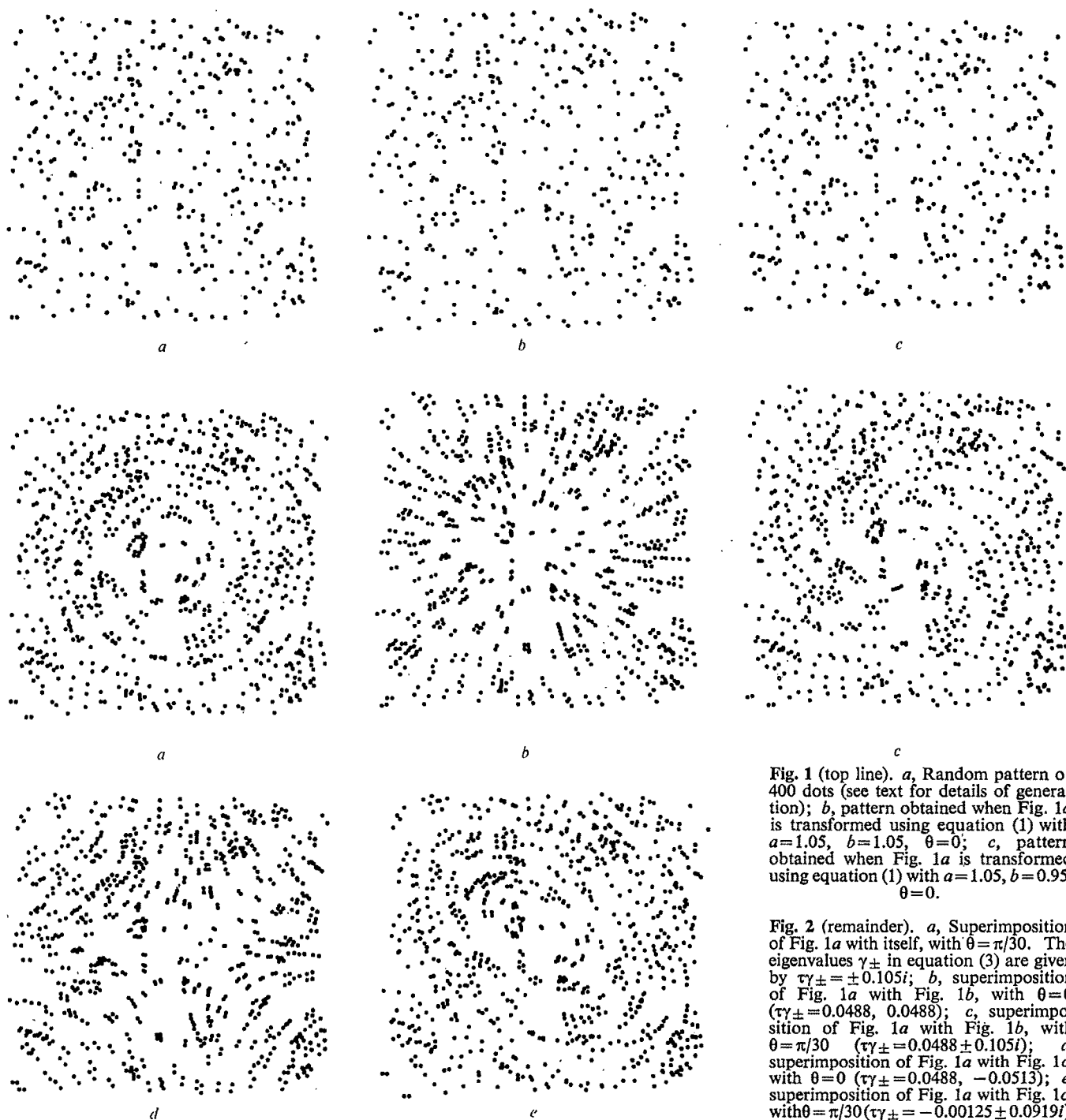


Fig. 1 (top line). *a*, Random pattern of 400 dots (see text for details of generation); *b*, pattern obtained when Fig. 1*a* is transformed using equation (1) with $a=1.05$, $b=1.05$, $\theta=0$; *c*, pattern obtained when Fig. 1*a* is transformed using equation (1) with $a=1.05$, $b=0.95$, $\theta=0$.

Fig. 2 (remainder). *a*, Superimposition of Fig. 1*a* with itself, with $\theta=\pi/30$. The eigenvalues $\gamma_{\pm}$ in equation (3) are given by $\tau\gamma_{\pm}=\pm 0.105i$; *b*, superimposition of Fig. 1*a* with Fig. 1*b*, with $\theta=0$ ($\tau\gamma_{\pm}=0.0488, 0.0488$); *c*, superimposition of Fig. 1*a* with Fig. 1*b*, with $\theta=\pi/30$ ($\tau\gamma_{\pm}=0.0488\pm 0.105i$); *d*, superimposition of Fig. 1*a* with Fig. 1*c*, with $\theta=0$ ($\tau\gamma_{\pm}=0.0488, -0.0513$); *e*, superimposition of Fig. 1*a* with Fig. 1*c*, with $\theta=\pi/30$ ($\tau\gamma_{\pm}=-0.00125\pm 0.0919i$).

equation, $\gamma_{\pm}$, by the relation³

$$\gamma_{\pm} = (1/\tau) \ln \Gamma_{\pm} \quad (3)$$

where τ is a non-negative, real constant

The dot interference patterns given in Figs 2*a-d* correspond to the only possible morphologies for two coupled, autonomous, first order, linear differential equations (or non-linear equations with non-zero linear terms) in the neighbourhood of a critical point and are called, respectively, a centre ($\gamma_{\pm}$ are pure imaginary), a node ($\gamma_{\pm}$ are real with the same sign), a focus ($\gamma_{\pm}$ are complex conjugates), and a saddle point ($\gamma_{\pm}$ are real with opposite signs)². If Figs 1*a* and 1*c* are superimposed and rotated the theory predicts that for $\theta > \sin^{-1} 0.05$, a focus will result, and this is observed (Fig. 2*e*). (For rotations in the range $2 \sin^{-1} 0.025 < \theta < \sin^{-1} 0.05$ there is a node, but as this comprises an angle of approximately $(0.025)^3$ rad or about 3 arc s it is not easily observed.) For any other differentiable transformation of the random dot pattern, the perceived

formed image correspond to the patterns generated by the trajectories of an underlying differential equation. This suggests that random dot interference patterns can be used to obtain qualitative information about the trajectories of first order differential equations of two variables. (The coordinates of each point in Fig. 1*a* were generated using a pseudorandom number generator (the RAND subroutine of FORTRAN IV implemented on an IBM 360 computer). The coordinates of the points in Figs 1*b* and 1*c* were then computed using equation (1). Figs 1*a-c* were plotted in a 6 x 6 inch area using a Calcomp plotter which printed an asterisk centred at each coordinate locus to ± 0.01 inch. To improve presentation, Figs 1*a-c* were drafted by hand from the computer printout. Transparencies of Figs 1*a-c* were made and these were superimposed to give Figs 2*a-e*. In the drafting process errors of approximately $\pm 1/16$ inch were introduced in the coordinate positions. By inspection of the interference patterns, in particular Figs

The perception of random dot interference patterns requires integration of the correlated signals over a large portion of the visual field. This can be shown in a variety of ways. If all but a small region of the pattern (which is, however, large enough to contain several correlated pairs) is occluded, the structure of the unoccluded region can no longer be perceived. By selective attention the viewer will notice several local features which arise as a result of the random generation procedure, but which are generally overlooked when the global organisation is perceived. Calling the length of one side of Fig. 2a, L , it can be shown that for a point at a distance $3L/8$ from the centre (where the circular pattern is readily seen), the number of uncorrelated points lying closer to a given point than the correlated point is approximately four. This shows that information from several pairs of correlated points must be integrated to detect the local correlations.

Transparent negatives of the patterns in Fig. 1 were made and correlated pairs were mounted so that when the images were projected using a stereoscopic projector and viewed without polaroid glasses, the negative images of the patterns in Fig. 2 could be seen. The intensities of each dot pattern could then be varied independently by rotating polarizers in the optical path. Consider the superimposition of Fig. 1a with itself, where the two patterns are labelled P and P', with P' rotated clockwise with respect to P: as the intensity of P' decreases with respect to P the entire figure appears to rotate in an anticlockwise direction; as the intensity of P' increases with respect to P a clockwise rotation is seen. Analogous results occur from the superimposition of the other pairs of figures used to construct Fig. 2. For example, calling Figs 1a and 1b, P and P', respectively, we find that decrease of intensity of P' results in a perceived contraction of the figure, while increase of the intensity of P' leads to a perceived expansion of the figure. For each case, although there is no real motion, there is a perceived apparent motion which can be described by saying that we perceive the movement of the centre of intensity of each pair of correlated points. Partial changes of intensity lead to partial motions. Although the perceived apparent motion is similar to the familiar "phi phenomenon"⁴, important differences distinguish the two effects. First, we have unsuccessfully attempted to observe partial motion as a result of incomplete intensity changes for the phi phenomenon, and have also been unable to locate any other reports in the literature of partial motion for this effect. Second, the motion effect described here requires a large region of correlated pairs of dots. If only a small portion of a pattern is presented, the effect disappears, mimicking the disappearance of perceived patterns of Fig. 2 under presentation of a small portion of the pattern. Over a wide range of intensity differences of the two subpatterns, the patterns of Fig. 2 can still be perceived. At very low intensities of one pattern with respect to the other, the patterns of Fig. 2 can, however, no longer be perceived and a random pattern is observed. The motion effect is particularly striking using the more easily generated splatter patterns presented in ref. 1.

The colours of each of the subpatterns of Fig. 2 can also be changed independently by interposing coloured filters in the optical path. The effects previously described remain unchanged. The patterns of Fig. 2 as well as the apparent motion effect can still be observed when the two subpatterns are of different colours. In addition, the resulting patterns give a striking presentation of the colour stereo effect⁵⁻⁷, in which different colours appear in different depth planes as a consequence of chromatic aberration of the eye; the effect is strongest with red and blue filters and low light intensities.

The patterns of Fig. 1 were presented binocularly as random dot stereograms (Julesz patterns)⁸. Negative slides for use with the stereoscopic projector, as well as positives which can be fused directly (or by using a stereoscopic viewer), were prepared. Initial experiments were performed using a random pattern and its rotated image. Using this stimulus it is possible that

both subpatterns into correspondence. To eliminate this possibility slides were prepared with vertical and horizontal axes passing through the centre of both the original and its rotated image. When these slides were projected and viewed without polarising stereo viewers, a circular pattern intersected by a single set of orthogonal axes is observed. Upon binocular presentation (with polarising glasses) the circular pattern disappears. The coordinate axes are fused, and with stereopsis a single set of random points are perceived lying on a tilted plane passing through the horizontal axis. No peripheral eye movements can bring the other subpatterns, presented as stereo pairs, into correspondence. Stereopsis can be readily performed with Figs 1a and 1b and also with Figs 1a and 1c. In each case, the interference patterns of Fig. 2 are destroyed and a single pattern of dots seen in depth is always perceived. In binocular presentation of random dot stereograms, cross correlations between the images in the eyes are computed with any disparities leading to depth perception. (See ref. 8, especially Figs 2.8-8, 6.5-3 and 6.5-4 and related discussions.) In binocular fusion of the patterns the small errors introduced by hand drafting are particularly noticeable and can be seen as small deviations away from the smooth surfaces defined by the disparities.

A major problem facing neurophysiologists is the determination of the physiological basis of form perception in higher animals. Major steps forward have been made in elegant demonstrations of cortical units which respond to a variety of local features in the visual field: stationary oriented stimuli⁹, moving oriented stimuli^{9,10}, and disparities between oriented stimuli in the right and left eyes^{11,12}. Although the demonstration of local feature extractors at the cortical level is suggestive, this demonstration is in itself insufficient to show the involvement of these units in perception processes requiring integration of local features to form global percepts. Further, few data are available concerning neutral units sensitive to global parameters of the visual input. The random dot interference patterns and stereograms provide uniquely simple stimuli in which local correlations must be integrated to form global percepts and in which both local and global features of the patterns can be independently varied. The use of these patterns as input stimuli in physiological experiments seems justified.

L. G. thanks Professor H. C. Longuet-Higgins for helpful conversations. We thank Professor John Lott Brown for conversations and loan of equipment. This research has been partially supported by a grant from the National Science Foundation.

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When immunogenetics was launched as an independent scientific discipline some 50 years ago, it represented hardly anything more than an application of Mendelian principles to inheritance of various blood groups in different species of mammals. Since that time, however, the study of immunogenetics has expanded considerably and in the last four or five years it has emerged as one of the leading disciplines in modern biology. In a way, immunogenetics today is in the same position as molecular biology was in the 1950's, revolutionizing our ways of thinking and linking together seemingly unrelated fields of modern biology and medicine. This development has far-reaching implications for medical sciences, particularly in the area of genetic control of disease

susceptibility, organ transplantation, and cancer. The rapid evolution of immunogenetics has been accompanied by a dramatic increase in new information. Until recently, this information has been scattered over many journals devoted primarily to other disciplines, such as basic immunology, genetics, cellular biology, virology, tumor biology, etc. With the intention of drawing together this growing body of information, "IMMUNOGENETICS" is being initiated. The scope of the journal will be the following:

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BOOK REVIEWS

Why a Textbook?

The Special Theory of Relativity. By H. Muirhead. Pp. xi+163. (Macmillan: London and Basingstoke, September 1973.) £3.95 boards; £2.45 paper.

DR MUIRHEAD describes this as "a textbook on special relativity from the high-energy physicist's point of view". He expresses surprise that "no undergraduate textbooks on special relativity have been written by high-energy nuclear physicists". Although his own attempt is enterprising and courageous, I hope it is not too unkind to suggest that it rather demonstrates why this should be the case. For the problems of high-energy physics for which special relativity concepts are important are problems for which much more difficult quantum concepts are even more characteristically important. By the time a student is ready to tackle the quantum ideas, he ought to be able to use special relativity almost without thinking. To attempt to teach special relativity to undergraduates with emphasis on applications to high-energy physics, with all respect to an expert in such physics, does appear to be doing things the wrong way round. The attempt inevitably results in the need to say of one topic that it "can only be properly appreciated within the framework of quantum mechanics", of another that "the story is complicated and we shall not pursue it here", and so on. Thus at best the student can only half understand what he is reading about. Actually Dr Muirhead does his best to cope with this situation by providing a set of carefully chosen "problems" at the end of each chapter, so that the student can at any rate test his understanding. And, of course, not every application discussed has a bias towards high-energy physics; for instance section 3.6, "The visual appearance of rapidly moving bodies", is an interesting simple topic that happens not to find a place in most textbooks and it seems to have inspired the publisher's attractive jacket design.

As a text on special relativity, a reviewer is bound to remark upon some shortcomings. There is no clear pattern to the mathematics; some deals with space and 3-vectors together with time, some with space-time and 4-vectors, and there is fragmentary use of matrices and tensors. Some of the derivations are laboured and confusing, as for example that of the Lorentz force in section 6.5. While the printing is clear, the layout is in some respects curiously inelegant

and there are numerous misprints—on page 125 a publishing house is called →ergamon →ress. A book of this sort makes one wonder why any textbook on special relativity is still needed. For special relativity is not a department of physics but a basis for nearly all physics. Almost everything that is known about it has been known for nearly seventy years; so one would think that by now it ought to have been absorbed into the general formulation of physics as a whole. How is it, then, that students still have to learn special relativity much as their predecessors have done over the past seventy years? They first become imbued with all the ideas of classical physics, and afterwards some of them acquire some small text that conveys to them how certain of these ideas may be somewhat unsatisfactory although this may be unimportant unless they have to play around with speeds approaching light-speed. And nearly every such text, that under review being no exception, starts with the same sort of historical introduction that has been the fashion from the start. So the reader's mind is conditioned to find relativity surprising and not quite "natural".

A simple partial answer is, naturally, that non-relativistic physics is so successful for most of what interests most people that these people have no practical need for anything else. And the comparatively few who do need relativity for practical purposes can get along by learning to use "relativistic equations of motion" without troubling about the rest of the subject.

To go a little deeper, while relativistic electromagnetism can be made simpler than non-relativistic, relativistic mechanics is much less simple than non-relativistic and, of course, the electromagnetic field may be observed only through its mechanical effects. Since then relativistic mechanics is not included in most elementary treatments of mechanics, one must rather grudgingly admit that a textbook of special relativity is still needed. Only let it be of some logical form and mathematical elegance, and without a historical introduction!

Maybe the best preparation for learning special relativity would be provided if someone nurtured upon relativity would write a textbook of general classical physics. He could have fun formulating postulates on rigid bodies, clocks, electromagnetic fields, and so on, so as to construct a self-consistent system yielding all pre-relativity physics—even including the paradox that if two twins separate and meet again after

completely different careers their ages must nevertheless be the same. Most readers would then turn with relief to relativity physics.

W. H. MCCREA

Brainwaves

Explorers of the Brain. By Leonard A. Stevens. Pp. 330 (14 plates). (Angus and Robertson: London and Sydney, 1973.) £2.95.

I FIND this book very attractive. It is a most readable and lively text enriched by a wealth of stories and anecdotes that are surprisingly accurate in all the fields in which I can check them. The author has made a remarkably erudite study of the history of brain exploration from Greek times to the present. He has travelled very widely in the United States, visiting a large number of laboratories which he lists in the acknowledgments section. Understandably his writing is coloured by the experiences he has had and the advice he has been given in these various centres for brain research. Nevertheless when he is dealing with important work in other countries, he is also very well informed. I am able to judge this in some fields in which I have personal experience as, for example, the Loewi-Dale story of chemical transmission and the Hodgkin-Huxley-Katz-Cole-Curtis story of the action potentials of giant axons. He gives a very well informed account of the EEG and the role of Hans Burger in this remarkable discovery.

Of particular value is his account of Ramón y Cajal whom he quite rightly makes one of the heroic explorers of the story. As in the case of Ramón y Cajal the chapter often starts with some remarkable event vividly told, and then it runs through a flashback of the scientific discoveries that led to this initial vivid scene. In this dramatic way, he is able to hold the interest of the reader.

Of course, in such a wide field as brain research, there must be many omissions of distinguished investigators. For example, there is no mention of Lucas, Zotterman, Mountcastle, Hubel, Wiesel, or Kuffler. In part these omissions arise because the very important afferent side of nervous pathways has been virtually ignored. On the other hand, there are superficially exciting scientific claims that have an undue treatment in the text. No doubt the author feels that these stories are valuable in his efforts to stress the play and interplay of scientific ideas in the growing fringes of brain investigations.

These are of course minor criticisms, and I would like to conclude by recommending the book very widely to all students of the brain and to all those interested in the history of the remarkable discoveries that have been made in this field: I have myself recommended it to my research associates. It is too often a temptation to the young investigator to narrow his field of interest unduly. A book such as *Explorers of the Brain* will open to him most attractive vistas in this immensely exciting field.

J. C. ECCLES

Clouds of Glory

Early Human Development. Edited by S. J. Hutt and Corinne Hutt. Pp. viii + 362. (Oxford University: London; Clarendon: Oxford, June 1973. £2.75 boards; £1.50 paper.)

THIS book should be called "Readings in Early Human Development". It reprints twenty-nine papers (some mercifully shortened), grouped in seven sections. Each section has a brief but well documented introduction. Most of the papers are without summaries. There is a perfunctory subject index, but no index of authors.

The first section, on genetical influences on behaviour, begins well. The editors give as the important general questions, "How much of the variance of scores on a particular trait under certain environmental conditions can be attributed to genetic factors? How modifiable is the phenotypic expression of such a trait? How do genetic and environmental influences interact?" Unfortunately, in the introduction to section 5, they drift into the usual confusion between genetical and ontogenetic determination; but this is only a minor lapse.

After the genetical section, three papers deal with hormones and behaviour. The third describes some unexpected findings which suggest that dosing a pregnant woman with progesterone can accelerate the early physical development of her child and can later enhance his intellectual development. The next section, entitled "Early Brain Mechanisms", is inevitably gravelled for lack of matter. It includes a study of rhythms of sleep and waking, and one on the effect of cycles of internal state on responsiveness to external stimulation.

Perception is covered by three papers on vision and one on auditory discrimination. The recent important work on the effects of errors of refraction on the development of vision was perhaps published too late for inclusion.

Two sections, under the headings of "Attachment" and "Early Experience", include papers on maternal deprivation. A classical paper by John Bowlby, "Maternal Deprivation in the First Year", is included.

cluded; and there are more recent and more critical studies in the same field, notably one by H. R. Schaffer entitled "Maternal Deprivation or Perceptual Deprivation?". Another paper discusses the reversibility of the effects of early lack of mothering. But some important investigations, which attempt to relate the precise nature of the deprivation to subsequent development, are not represented.

Finally there are six papers on stimulation in early life and on the development of fear. These illustrate, among other things, the importance of this topic and how much remains to be learnt about it.

This is a useful collection. It includes papers which illustrate some of the many methodological hazards of work in this field. It would have been still more useful if the editors had written more, and so filled some of the gaps. Among special but important items not adequately covered are researches on sucking and — still more notable — investigations of intellectual development in the first year. The editors seem to have some doubts about the usefulness of cross-cultural studies, and they are not represented. These include findings, on the influence of social class on development, which ought to influence social policy. But if, as the editors rightly assume, comparisons with other species can suggest testable hypotheses about man, then comparisons of human groups can do so too.

Despite omissions, some of them no doubt inevitable, this volume gives a helpful and instructive picture of a region of study which is now full of life and could hardly be more important.

S. A. BARNETT

The Airport Affair

A Sadly Mismanaged Affair: A Political History of the Third London Airport. By David McKie. Pp. 256. (Croom Helm: London, October 1973.) £3.75.

DAVID MCKIE, of *The Guardian*, tells a lively tale of the political problems of deciding where London's third airport should go. In 1944 Lord Swinton, Minister of Civil Aviation, had been able to say of Heathrow that it was the "only possible site" for London's airport. No one is so sure about anything in 1973. The book takes us briskly through Croydon, Heathrow, Gatwick, Stansted, Cublington, Thurleigh, Nuttampstead and Foulness, and it is clear, after the inquiries and committees, that it is possible to prove anything once the terms of reference are designed properly. Even so, an airport seems to be one monument to which politicians don't crave to have their names attached.

Roskill is viewed with some awe and

it must be said, doesn't come over very clearly. One senses that Mr McKie has not really tried to understand the technical side of the issues at all, as is his privilege in what he calls a political history. Nevertheless, this does make the book somewhat unsatisfactory. There are no figures on the predictions and realities of usage of airports, on the impact of wide-bodied jets on airport planning, on the levels of noise at varying radii from airports, on the improved noise performance of modern engines and on many other technical issues. The reason that the planning process has been so tortuous is not simply that there have been local objections; the technical ground has been shifting continuously under the politicians' feet. The book is incomplete, however readable, without the driving forces being in clearer focus.

D. DAVIES

Plasmids

Bacterial Plasmids: Conjugation, Colicinogeny and Transmissible Drug-Resistance. By G. G. Meynell. Pp. xiii + 164. (MIT: Cambridge, May 1973.) \$14.99.

DURING the past decade there has been a considerable expansion in the study of bacterial plasmids. From the early days, when the plasmid F served as a mere tool for unravelling the intricacies of *Escherichia coli* genetics, their importance has increased concomitant with the realisation that quite unrelated plasmids are of relatively frequent occurrence in many bacterial genera, and that in many cases they have the ability to cross interspecies and intergeneric boundaries. Combined with their ability to carry genes determining resistance of the host to antibiotics, these properties give them great medical importance, while their ability to transfer host chromosomal genes suggests that they may play a significant role in the evolution of bacterial species.

There will therefore be wide interest in this book, which sets out to review the important biological characteristics of bacterial plasmids. The three central chapters (chapters 5, 6 and 7) deal with their transmission from cell to cell by conjugation, their replication within the cell as autonomous DNA molecules, and the physical properties of these molecules. These chapters provide a brief but adequate introduction to plasmid biology, although, inevitably for a book written two years ago about a rapidly-expanding field, much important recent information is absent. In particular, the chapter on conjugation is noticeably out of date, and topics such as the discovery of a large number of plasmid incompatibility groups, and the use of electron microscope heteroduplex tech-

niques for physical studies of plasmid molecules, are necessarily but unfortunately missing.

The discussion of plasmid-host chromosome interactions in chapter 3 is less satisfactory, because of its heavy dependence upon analogies with λ phage—which I consider to obscure, rather than clarify, the properties of transmissible plasmids. In other places, the text could have been lengthened with advantage; for example, the accounts of plasmid-determined characters in chapter 7 are really too short to be useful, and surprisingly little attention is paid throughout to plasmids other than those found in the Enterobacteriaceae.

Despite omissions and occasional obscurities, the book provides an introduction to the biological properties of bacterial plasmids, and an extensive bibliography, that medical and science students will find of value. The requirements of the research worker, however, will be better satisfied by the recent spate of review articles.

N. S. WILLETS

Hydra

Biology of Hydra. Edited by Allison L. Burnett. Pp. xv+466. (Academic Press: New York and London, May 1973.) \$29.

THE title of this book gives the impression that its scope is wider than in fact is the case. Of the sixteen chapters, twelve are concerned with developmental topics, including discussions of the developmental significance of interstitial cells, organismic polarity, histological and ultrastructural studies of the development of nerve cells and of cyto-differentiation during regeneration, cell proliferation in relation to form and the structure and developmental significance of the mesogloea. The remaining chapters are devoted to behaviour, feeding and digestion, ecology and neuro-secretory cells. The emphasis on developmental studies is a fair reflection of the distribution of research activity in recent years.

Although it is nowhere made explicit, all the contributors (with one possible exception) are present or former students and colleagues of the editor; this gives the book a somewhat parochial air. The contributions are rather a mixed bag. Among the more useful I would single out Rushforth's introductory survey of behavioural studies which is clearly written and informative; and Diehl's discussion of interstitial cells, which I hope will at last put an end to the arguments about the morphogenetic role of these cells (they have none) which have plagued the literature for so many years.

Some of the other contributions on developmental topics are of more doubt-

ful value and I would single out two for specific comment. The chapter on organismic polarity by Lesh-Laurie seems to me quite inadequate. This is an area in which significant progress has been made in recent years and general models have been developed which are applicable not only to *Hydra* but also to many other developing systems; in this respect there has been a genuine, if incomplete, synthesis. No-one reading this review would gain any hint of these advances, since the relevant literature is not cited. Admittedly, the most comprehensive discussions have appeared relatively recently, but Wolpert's theoretical discussion which appeared in 1969 is not quoted and no reference is made to the important experimental work of Rose on *Tubularia* which is now 16 years old.

Whereas I find the discussion of polarity merely inadequate, I must say that I regard the chapter devoted to cell proliferation in relation to morphogenesis as positively confusing and misleading. The points at issue are whether patterns of cell movement in the growing organism are to be explained in terms of patterns of cell production or in terms of patterns of cell loss and whether morphogenesis is to be explained in terms of localised cell proliferation or in other terms. The axial pattern of cell proliferation, so stressed in this chapter, is an important piece of evidence in this argument but by no means as decisive as the editor and author imply. The whole subject is treated in such a way that the uninitiated might get the impression that the ideas of other workers in the field—particularly those of Campbell, whose evidence and arguments are inadequately discussed—have been refuted. This is certainly not the case; Campbell's work remains as compelling as ever and the new data which Dr Corff presents at such length do not seem to me to constitute evidence which can be used one way or the other in this argument.

I do not think this book can be regarded as anything more than a convenient, if extremely expensive, summary of the work of the Burnett "school". The greater part of it is concerned with developmental problems but it is both too parochial and too defective in key areas to constitute a definitive survey of our present knowledge in this field. In terms of theoretical content the book is very weak; no formal models are discussed, though there are several in existence, and such theory as there is consists for the most part of vague speculation. In too many chapters the authors are content to present the reader with a mass of experiments and observations and leave him to draw his own conclusions as to its possible meaning.

GEOFFREY WILSON

Jobs for Graduates

Patterns of Change in Graduate Employment. Edited by H. Greenaway and G. Williams. Pp. 171. (Society for Research into Higher Education: London, September 1973.) £2.70.

"DESPITE the growing concern about the employment of graduates", say the editors of this collection of essays by different authors, "there has so far been little attempt to place the problem in perspective". Certainly much of the public discussion has been concentrated upon short-term variations in the pattern of supply and demand, particularly for newly-qualifying scientists and engineers. The difficulties of those in mid-career have received scant notice, and one of the best parts of the book is the chapter on this subject by W. G. H. Robins, who shows how relatively large this problem may be.

The nation is, however, committed to the continued expansion of higher education with over 20% of eighteen-year-olds, and over 25% of eighteen-year-old boys, entering higher education by 1981; these students will then be asking for and expecting jobs appropriate to their level of education. It is idle to pretend and dangerous to assume that this can happen without stresses affecting both the newly qualified and employers and their existing staffs, or that economic growth can, by itself, create sufficient jobs at the right level. A problem exists of a continuing nature proportional in size to the rate of change of the supply and demand situation, or more accurately to the value of the second differential.

In discussions of supply and demand, it should not be forgotten that here the supply is of human beings, with hopes, prejudices and fears, and Tom Snow writes perceptively about students and their problems in choosing their first occupations. There are other good things in the book, such as E. G. Whybrew's brief chapter and Gareth Williams's illuminating analysis of the economics of the graduate labour market, but some of the most disappointing parts are those for which the editors have been personally responsible. Their joint final essay "Is There a Crisis?" is unexceptionable but their early individual chapters suffer from obscurity, inaccuracy and lack of perspective. The roots of today's manpower situation lie deeper in the past than the Robbins Report of 1963; arguably for scientists and technologists they derive from the connection between fundamental and applied science and national security, and the line from 1940 to 1970 through the Manhattan project to the Apollo project is continuous. There has also been the belief that more research meant more economic growth, a belief which Robbins institutionalised

at a moment when it was no longer true. Harriet Greenaway's "Impact of Educational Policies" starts with Robbins and concentrates mainly on the past five or six years, with too much attention devoted to very recent happenings, some of them unimportant. First employment statistics are discussed by both editors separately in chapters 1 and 2; the reason for this is unclear, the tables are confusing and the total effect is more muddled than even this difficult subject need be. In spite of these defects this is a worthwhile book, and there is a useful six-page bibliography.

B. J. HOLLOWAY

Ectomycorrhizae

Ectomycorrhizae. Edited by G. C. Marks and T. T. Kozlowski. (Physiological Ecology: a Series of Monographs, Texts, and Treatises.) Pp. xiv + 444. (Academic: New York and London, June 1973.) \$28.50.

THE content of this latest volume on mycorrhizae, specifically ectomycorrhizae in this instance, reflects a revival of emphasis on the general biology of these structures. The emphasis is very much on the need to relate more carefully findings from controlled laboratory experiments to complex soil situations.

Many references are made to ectomycorrhizal synthesis. Well tried aseptic techniques are described and at the same time mention is made of the need to consider possible role(s) of rhizosphere microorganisms in synthesis and function. The inclusion of a specific rhizosphere chapter (by Rambelli) is excellent, but the chapter itself is a little disappointing both in presentation and in the errors it contains. The section on the concept of the rhizosphere is muddled, and the data of Buxton (1957) on page 323, Slankis *et al.* (1964) on page 318 and Rovira (1965) on page 314 are either incorrectly quoted or presented in a confused way. Also Figs 1 to 8 do not relate properly to the accompanying text.

Bjorkman's hypothesis, it is concluded by various contributors, is an oversimplification of the situation. The comments of Slankis on the probable involvement of growth hormones are very relevant and the concept of a mycorrhizal infection zone (MIZ), as outlined by Marks and Foster, should prove of value in further studies on the synthesis problem. The comments of Bowen and Theodorou on the need to separate the process of root surface colonisation from that of infection proper involving the formation of an Hartig net are also important.

Ectomycorrhizal function is also discussed at length. Bowen's contribution on mineral nutrition is quite excellent and his remarks on the need to study

soil situations such as form and mobility of ions in soils and the importance of mycelial strands are very logical. This author also mentions field inoculations and forestry practice. This more applied aspect of mycorrhizal studies is further developed by both Meyer and Mikola in their respective chapters. The possibility of conducting field inoculations with fungi suited to particular situations such as soil types and climate, and the necessity (or not) of raising nursery seedlings under conditions conducive to mycorrhizal infection, are discussed. Somewhat related to these points, perhaps in connection with the establishment of culture collections of useful ectomycorrhizal fungi, are the problems of their precise identification as discussed by Zak.

Marx deals with the function of ectomycorrhizae as protective agents against certain soil pathogens. Several contributors venture the opinion that nutrient uptake and protection against soil pathogens are the two important functions of ectomycorrhizae but that there are others.

The importance of nitrogen in ectomycorrhizal synthesis and function is mentioned many times but it is clear that much work still remains to be done on its general involvement. Its relative importance to phosphate is still not known. The same sort of comments are relevant to studies on the involvement of root exudates (and metabolites). Here it seems that too much emphasis has been put on aseptic laboratory experiments.

It is something of a relief to see the consistent use of the term ectomycorrhiza(e) throughout the book. I am less happy about the use of the terms obligate and facultative ectomycorrhizal tree as proposed by Meyer. Applying these terms ecologically, as he suggests, is virtually impossible.

Despite the inevitable variable quality of the chapters, most are excellent. The volume as a whole is well integrated and makes for consistently stimulating reading. It certainly rates as a significant contribution to the study of ectomycorrhizae.

B. W. FERRY

Decision and Reaction

Attention and Performance IV. Edited by Sylvan Kornblum. Pp. xxvii + 771. (Academic: New York and London, April 1973.) \$18.50.

THE series of volumes with this title forms one of the curious spontaneous developments of modern psychology. The first appeared six years ago; it reported the papers given at a small gathering of like-minded researchers organised in Holland by Andries Sanders. The gathering was fun; two more meetings followed in quick succession and each gave rise to its volume of

proceedings. Usually, volumes assembled from conference papers are uneven, badly edited, and packed with the output of those who need to give a paper to get their fare; but *Attention and Performance* was not like that. The three volumes have been eagerly read by advanced workers and students alike, and contain many of the basic papers in the newly expanding area of cognitive psychology. Now the fourth volume appears; this time the conference moved from Holland to the USA, the editor and publisher ceased to be Dutch, and the sheer thickness of the volume has increased. The question obviously arises, is the magic still there?

Briefly, it is. There are forty papers in the volume, and almost every one makes some point which needs consideration even if one disagrees with it. No journal has such a high success rate, and once again the book should be bought by anybody who wants to know what is happening at the frontiers of research into the areas covered. This time, the sections of the meeting were devoted to selective attention, physiological correlates of attention, sequential effects in reaction time and judgment, organisation of memory, and judgments of temporal order. There are also sections on two special aspects of reaction time, which are titled "binary classification" and "choice" respectively, but which might be better described as "experiments in which a person decides whether two patterns are the same or different" and "the relation between speed and accuracy in decision".

These areas are technical, and this is not a book for the amateur. In an attempt to widen its scope, each section starts with a "tutorial review" of the area, but it was perhaps too optimistic to expect first-rank workers to forget that at the meeting itself they were talking to the highly knowledgeable. The best review for outsiders is that by Vaughan and Ritter on the various cortical evoked potentials and their relationship to behaviour; runners-up are Kornblum on sequential effects and Nickerson on the "binary classification" task, provided one already knows why these topics are important. Other reviewers such as Moray and Fitter, Norman, or Audley used the occasion to put forward a general and highly original framework of their own for theorising in the particular area, and these might be positively misleading for the unguided novice. This departure therefore did not succeed in making the book into a true textbook. But was such an attempt worth while? The real virtue of *Attention and Performance* lies in the opportunity it gives for some of the brightest minds in psychology to strike sparks off each other at a technical level. Long may it continue.

DAVID F. PEARSON

Obituary

Selman Abraham Waksman

IN Woods Hole, Massachusetts, on August 16, 1973, the eminent Nobel laureate microbiologist, Selman A. Waksman, died suddenly of a cerebral haemorrhage. There, three days later, he was buried far from his native Russia but close to one of the laboratories he had helped to develop.

Selman Abraham Waksman was born on July 22, 1888, in the town of Priluka near Kiev in the Ukraine. Finding it difficult, as a Jew, to enter the University of Odessa, he left for the United States in 1910. The next year Waksman entered Rutgers College (New Brunswick, New Jersey) on a State scholarship. He received a Bachelor of Science in Agriculture in 1915 and was elected to Phi Beta Kappa, the first of the many academic honours his incredible intellectual industry would yield. The next year, at the same institution, Waksman received a Master of Science degree for work done under the supervision of Dr Jacob G. Lipman. In 1918 he received a PhD in biochemistry from the University of California in Berkeley. Except for part-time appointments at Cutter Laboratories in California and at Takamine Laboratories in New Jersey, Dr Waksman's whole career developed at Rutgers University where he was first appointed in 1918, and promoted to Professor in 1930. In 1940 he was named head of the Department of Microbiology of the College of Agriculture, and in 1949 he became Director and founder of the Institute of Microbiology of Rutgers University. He retired in 1958 but continued for many years to direct a limited amount of research.

Dr Waksman was a prolific writer. During his life he and his collaborators published more than 500 papers and twenty-eight books. This output ranged from booklets giving practical advice on the use of enzymes for such purposes as jelly-making, soil fertilisation, and mushroom growing, to erudite historical studies. Between these two extremes stands a mass of research communications centring around soil microbiology.

While still a student at Rutgers, Dr Waksman became interested in the ecology and the taxonomy of actinomycetes. At first, he thought of these organisms merely as decomposers of organic matter playing a key role in the building of humus and the modelling of the soil. However, in 1923, he and Robert L. Starkey wrote in *Soil Science*: "Certain actinomycetes produce substances toxic to bacteria, as shown by

Greig-Smith (in 1917) and as often observed in our work, when around an actinomycetes colony upon a plate, a zone is found free from fungus and bacterial growth."



In 1937, in collaboration with Jackson W. Foster and Imri J. Hutchings, he published in the same journal a series of papers on associative and antagonistic effects of microorganisms. Following the spectacular success of his former student, René J. Dubos, who discovered tyrothricin in 1939, as well as the revival of Alexander Fleming's penicillin by Ernst B. Chain, Howard Florey and associates in 1940, Dr Waksman concentrated on the study of antibiotics. A total of twenty-two antibiotics, mainly from actinomycetes, were isolated in his laboratory, four of which have been useful enough to be produced commercially for medical use. These are actinomycin, an antitumour agent, streptomycin and neomycin, active against bacteria and mycobacteria, and candicidin, an antifungal agent. Of these, streptomycin, isolated in 1944, is the most widely employed and its use revolutionised the treatment of tuberculosis and closed many a sanatorium. For the discovery of this compound, Dr Waksman was awarded the Nobel Prize in Physiology and Medicine in 1952.

Before becoming involved in the study of antibiotics, Dr Waksman concentrated on the role of microbes in the soil and in the building of humus. He was in turn an expert on microbial enzymes, autotrophic bacteria, especially sulphur bacteria, the formation and the use of peat, marine microbiology, the production of organic acids by fungi, the role of thermophilic organisms in composting, the taxonomy of actinomycetes, the role of heavy metals in the nutrition of fungi and the history of microbiology. In this last field, his

major contributions were biographies of Haffkine, Winogradsky and Lipman.

Dr Waksman organised the division of Marine Bacteriology at Woods Hole Oceanographic Institution in 1931 and for over a decade he contributed to our knowledge of the ecology of marine microbes. In the sea, as in the soil, he was concerned with the role of microorganisms in the decomposition of organic matter. He recognised that microbial activity decreased with an increase in depth. He considered fungi and actinomycetes to be soil organisms which may be only casually carried to the sea from their natural habitat on land. Upon his retirement from active research at Woods Hole Oceanographic Institution in 1942, he was elected a trustee and he served in this capacity until his death.

The bulk of the royalties received from the manufacturers of streptomycin and neomycin was used to establish an Institute of Microbiology which opened its doors in 1954. The original plan of Dr Waksman was to explore six major fields of research: general microbiology, microbial physiology, antibiotics, vitamins and enzymes, microbial ecology and applied microbiology. As the Institute developed, certain fields such as the study of vitamins were neglected while others were added. Among these were immunochemistry under the leadership of Michael Heidelberger, as well as other fields such as genetics and virology.

Dr Waksman was a link between microbiologists of the United States and of the Soviet Union. He wrote numerous articles on Russian scientists and their work and visited the Soviet Union several times.

Dr Waksman was of Jewish stock, and although not a religious man he was a keen scholar of Jewish history and institutions. He visited Israel on several occasions and played a key role in the creation of the Institute of General and Industrial Microbiology of the Technion of Haifa.

A short, stocky man with a perennially busy air, Dr Waksman loved to recount stories about his life and career. They were always pertinent to the discussion or lecture of the moment, and usually provided an historical or scientific insight for his listener. He was a loyal supporter of all those who had gained his confidence and who now mourn a departed friend.

Dr Waksman is survived by his widow, Deborah B. (Mitnik) Waksman, and his son Dr Byron H. Waksman, a distinguished immunologist who is Professor of Microbiology at the Medical School of Yale University.

Announcements

University News

F. Moreton and L. R. G. Treloar have been appointed Professor Emeritus by the University of Manchester.

Miscellaneous

Sir Martin Ryle, Professor R. R. Porter and Professor E. P. Abraham have been awarded the three Royal Medals of the Royal Society.

Erratum

In the article "Geomorphological Dating of Cave Opening at Makapansgat, Sterkfontein, Swartkrans and Taung" by T. C. Partridge (*Nature*, 246, 75; 1973), in the section "Nickpoint Migration", the first line should read "Figure 2 shows the locations of the sites . . .".

Corrigendum

In the article "Canadian Tropical Research in the West Indies" by Finn Sander (*Nature*, 244, 201; 1973), it was wrongly stated that the Bellairs Research Institute is the only Canadian teaching and research institute in the tropics. A similar research institute, attached to the University of Montreal, and stressing studies in anthropology and sociology, functions in Martinique. The author expresses his apologies to the University of Montreal.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

- Mineral Resources Consultative Committee. Mineral Dossier No. 7: Salt. By A. J. G. Notholt. Pp. vi+36. (London: HMSO, 1973.) 47p net. [127]
- Ospreys and Speyside Wildlife. Pp. 42. (The Lodge, Sandy, Bedfordshire: The Royal Society for the Protection of Birds, 1973.) 40p. [137]
- Department of the Environment. The Welsh Office. River Pollution Survey of England and Wales, Updated 1972. Discharges of Sewage and Industrial Effluents. Pp. xi+20. (London: HMSO, 1973.) 50p. [137]
- King Edward's Hospital Fund for London. Annual Report. Pp. 32. (London: King Edward's Hospital Fund for London, 14 Palace Court, W2, 1973.) [137]
- BBC Programmes Complaints Commission. Annual Report, 1972-73. Pp. 11. (London: BBC Programmes Complaints Commission, 1973.) [167]
- The National Institute of Agricultural Botany. Fifty-third Report and Accounts, 1972. Pp. 83. (Cambridge: National Institute of Agricultural Botany, Huntingdon Road, 1973.) [167]
- Medical Research Council. National Institute for Medical Research—Scientific Report for 1971-72. Pp. v+114. (London: Medical Research Council, 20 Park Crescent, W1, 1973.) [167]
- Scottish Plant Breeding Station. Fifty-second Annual Report, 1972-73. Pp. 82. (Pentlandsfield, Roslin, Midlothian: Scottish Plant Breeding Station, 1973.) 25p. [167]
- Proceedings of the Royal Irish Academy. Vol. 73, Section A, No. 8: A Note on the Escape of Neutrons from Within Einstein's Spherical Cluster of Gravitating Masses. By P. A. Hogan. Pp. 91-97. 14p. Vol. 73, Section A, No. 9: Cumulative Results of Testing a Meteorological Mathematical Model—The Description of the Model. By K. Miyakoda. Pp. 99-130. 63p. Vol. 73, Section B, No. 9: Synthesis of Halogenated Heterocyclic-Substituted Chromosomes and Related Compounds. By D. J. Donnelly, J. A. Donnelly and E. M. Philbin. Pp. 129-132. 14p. Vol. 73, Section B, No. 10: Observations on the Growth of Ephemeroptera in Fluctuating and Constant Temperature Conditions. By Edward Fahy. Pp. 133-149. 26p. (Dublin: Royal Irish Academy, 1973.) [167]
- Pay Board. Report 2 April-31 May 1973. Pp. vi+12. (London: HMSO, 1973.) 13½p net. [167]

Other Countries

- World Health Organization. Public Health Paper, No. 52: Development of Educational Programmes for the Health Professions. Pp. 103. (Geneva: WHO; London: HMSO, 1973.) 7 Sw. francs; 90p; \$2.10. [237]
- Stockholm International Peace Research Institute. SIPRI Research Report No. 11: Ten Years of the Partial Test Ban Treaty, 1963-1973. Pp. 34. (Stockholm: Stockholm International Peace Research Institute, 1973.) [237]
- Sveriges Geologiska Undersökning, Stockholm. Lovo Geomagnetic Observatory—Year Book 1971. Pp. 36. (Stockholm: Sveriges Geologiska Undersökning, 1973.) [237]
- World Health Organization. Technical Report Series, No. 527: Advances in Methods of Fertility Regulation—Report of a WHO Scientific Group. Pp. 42. (Geneva: WHO; London: HMSO, 1973.) 4 Sw. francs; 50p; \$1.20. [247]
- Australia: Commonwealth Scientific and Industrial Research Organization. Annual Report of the Division of Applied Chemistry, 1971/1972. Pp. 68. (Melbourne: CSIRO, 1973.) [257]
- United States Department of the Interior: Geological Survey. Professional Paper 729-A: Geology of Pre-Tertiary Rocks in the Northern Part of Yellowstone National Park, Wyoming. By Edward T. Ruppel. Pp. vi+66. (Washington, DC: Government Printing Office, 1972.) [257]
- Geological Survey of Canada. Geology Map 1348A: Greely Fiord East, District of Franklin. (Ottawa: Geological Survey of Canada, 1973.) [267]
- Berichte des Deutschen Wetterdienstes. Nr. 130 (Band 17): Untersuchungen über Kleinräumige Änderungen des Kaltluftflusses und der Frostgefährdung durch Strassenbauten. Von Erwin King. Pp. 24. (Offenbach a.M.: Selbstverlag des Deutschen Wetterdienstes, 1973.) [267]
- National Botanic Gardens of South Africa. Report, 1971-1972. Pp. 56. (Cape Town: National Botanic Gardens of South Africa, 1973.) [267]
- Australia: Commonwealth Scientific and Industrial Research Organization. Division of Soils Technical Paper No. 17: Computer Program for Use in Electron-probe Microanalysis when Some Concentrations are Known. By A. C. Oertel. Pp. 5. (Melbourne: CSIRO, 1973.) [277]
- Fondation Universitaire, 52e Rapport Annuel, 1971/1972. Pp. 68. (Bruxelles: Fondation Universitaire, 1973.) [277]
- Commissariat à l'Énergie Atomique. Rapport Annuel 1972. Tome 1. Pp. 90. Tome 2. Pp. 207. (Paris: Commissariat à l'Énergie Atomique, 1973.) [277]
- Australia. CSIRO. Serial Publications, Monographs, and Pamphlets issued by CSIRO. Pp. 106. (East Melbourne: CSIRO, 1973.) [277]
- Public Policy Toward Environment 1973: A Review and Appraisal. (Annals of the New York Academy of Sciences, Vol. 215.) Pp. 202. (New York: New York Academy of Sciences, 1973.) [307]
- United States Department of the Interior: Geological Survey. Professional Paper 732-B: Scour and Fill in Tujunga Wash—a Fanhead Valley in Urban Southern California—1969. By Kevin M. Scott. Pp. iii+29. (Washington, DC: Government Printing Office, 1973.) 70 cents. [307]
- Organization for Economic Co-operation and Development, Paris. Environment Directorate. Report and Conclusions of the Joint ad hoc Group on Air Pollution from Fuel Combustion in Stationary Sources. Pp. vi+211. (Paris: OECD, 1973.) [307]
- Sveriges Geologiska Undersökning. Arsberättelse för År 1972. Pp. 54. Avhandlingar och Uppsatser. Ser. C. Nr. 679: Late-Glacial and Pre-Boreal Pollen and Diatom Diagrams from Skurup, Southern Scania. By Ann-Marie Robertsson. Pp. 75. Nr. 680: Indications of a Litorina Transgression in the Nyköping Area. By Christer Persson. Pp. 23. Nr. 682: Doda Fallen I Avesta. By Jan de Geer. Pp. 37. Nr. 683: The Lower Viruan in the Autochthonous Ordovician Sequence of Jamtland. By Kent Larsson. Pp. 82. Nr. 684: Postglacial Transgressions in Bohuslän, Southwestern Sweden. By G. Persson. Pp. 47. Nr. 689: Structural Geology of the Marsfjällen Area, Caledonides of Västernorrland, Sweden. By R. A. J. Trouw. Pp. 115. (Stockholm: Sveriges Geologiska Undersökning, 1973.) [307]

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(1833)

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(1924)

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£2,600 to £4,900 for a single man

£3,200 to £5,950 for a married man with two children.

Other benefits include free passages, liberal leave on full salary, generous education allowances, Government quarters at moderate rental. Appointment Grant up to £200, Car Advance £600, may be payable.

The post described is partly financed by Britain's programme of aid to the developing countries administered by the Overseas Development Administration of the Foreign and Commonwealth Office.

For further particulars you should apply, giving brief details of experience to:

crown agents

M Division, 4 Millbank, London SW1P 3JD, quoting reference number M3F/730720/NF.

(1899)

THE GERMAN CANCER RESEARCH CENTER HEIDELBERG

(Foundation of Public Law)

REQUIRES for the INSTITUTE OF VIRUS RESEARCH

A qualified and cooperative Scientist for the Sector RNA—Tumor—Viruses

Requirements:

It is expected that the applicant will establish an RNA-Tumor virus group, therefore, he should be experienced with both biology and molecular biology of RNA tumor viruses.

Offers:

Salary group AH3 provided the applicant fulfils the conditions of German Civil Service, otherwise corresponding grade of employment; modern laboratory facilities in new building, assistance with finding accommodation.

Only written applications will be considered. They should be submitted with a complete list of publications and curriculum vitae to the administration of the Deutsches Krebsforschungszentrum, 69 Heidelberg, Kirschnerstrasse 6, by 31st March 1974 and should be marked "Berufungsausschuss".

(1907)

Department of Education and Science International Scientific Liaison Scientist/Technologist

with wide interests in the role of science and technology in modern society. To be concerned with promoting UK participation in the programmes of inter-governmental organisations concerned with science, such as UNESCO and OECD.

The successful candidate will conduct studies, contribute to policy papers, and prepare briefs for UK representatives at meetings abroad. The work involves consultation with a wide range of bodies in this country and overseas. The post is in London although short trips abroad will be required from time to time.

Candidates (aged between 25 and 32) should have a First or Second Class Honours degree in a scientific or technological subject, and at least four years' postgraduate experience in industry, government, or the academic world. Considerable ability in presenting ideas clearly and persuasively, both in writing and orally, is called for. A working knowledge of French, though not necessarily fluency, is desirable but not essential.

Appointment will be as Senior Scientific Officer (£2,790-£3,815).

Application forms (to be returned by 4 January 1974) from Miss B. C. Taylor, Room 8/18 Tower Block, Department of Education and Science, Elizabeth House, 39 York Road, London SE1 7PH, telephone 01-928 9222 ext 2237, please quote SA/1/G/2.

(1870)

UNIVERSITY OF LEICESTER DEPARTMENT OF ASTRONOMY AND HISTORY OF SCIENCE

Applications are invited from men and women graduates for a TUTORIAL ASSISTANTSHIP in the HISTORY OF SCIENCE in the Department of Astronomy and History of Science. Applicants will be expected to work on some aspect of the social relations of science, or on related areas in the history or philosophy of science.

Salary scale: £1,353 to £1,632 a year.

Further particulars from the Registrar, to whom applications should be sent by December 21. (1835)

CHELSEA COLLEGE UNIVERSITY OF LONDON

TECHNICIAN GRADE 2A required in the Microbiology Section of the Biological Sciences Group. Duties will include assisting in the preparation of media, reagents and cultures for undergraduate teaching and postgraduate research activities. Previous experience in microbiology (bacteriology, mycology, virology) is required. Salary scale: £1,552 to £1,822 per annum (including London Allowance).

Application forms from Mr K. Harris, (N) Department of Applied Biology, Chelsea College, Hortensia Road, London SW10 0QX. (1840)

UNIVERSITY OF BOTSWANA, LESOTHO AND SWAZILAND

Applications are invited for (a) SENIOR LECTURESHIP or (b) LECTURESHIP IN STATISTICS on the Botswana Campus in Gaborone. Candidates must hold a Master's degree in Statistics or related subject such as Economics or Mathematics with Statistics as a major subject. They should have proven research ability and both teaching experience and practical knowledge of the type of work of statistical offices in developing countries. Special interest in demography is desirable. Salary scales: (a) R4,404 to R5,664 per annum; (b) R3,204 to R4,764 per annum (£1 sterling=R1.60). A 25 per cent gratuity is paid in lieu of superannuation. The British Government may supplement salaries in range £375 to £825 per annum (sterling) for married appointee or £150 to £425 per annum (sterling) for single appointee (normally free of all tax) and provide children's holiday visit passages. Education allowance; accommodation at reasonable rents; family passages; overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail, not later than January 4, 1974, to the Registrar, University of Botswana, Lesotho and Swaziland, Roma, Lesotho, Africa. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (1843)

(RE-ADVERTISEMENT)

NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING (UNIVERSITY OF READING)

Applications are invited for a post of SCIENTIFIC OFFICER in the Bacteriology Department to assist in the Maintenance of the National Collection of Dairy Organisms and in Research in the field of Bacterial Systematics. The work is presently concentrated on the enzymatic and DNA composition of Bacteria. Applicants should preferably have an interest in bacterial physiology and some expertise in biochemical techniques.

An appropriate degree, H.N.D., H.N.C. or equivalent qualification is required. Salary £1,318 to £2,177 with a starting point dependent on qualifications and experience. Superannuation, with an allowance to offset contributions.

Apply on forms obtainable from the Secretary, N.I.R.D., Shinfield, Reading RG2 9AT. Quote reference 73/76. (1834)

Engineer or Applied Mathematician

The Royal Dutch/Shell Exploration & Production Laboratory at Rijswijk, near The Hague, the Netherlands, has a vacancy at short notice for an engineer or applied mathematician.

Knowledge/Experience

He will have a sound knowledge of elasticity theory, a background in continuum mechanics and experience in modern computational methods, in particular finite elements. Some experience in rock mechanics would be welcome.

Job

Elastic/plastic analysis of tectonic models, working in a team of physicists and geologists.

Preferred age: 25-35.

Travelling and other reasonable expenses will be paid for interviews in London and The Hague. We will give financial assistance with the removal of household effects to Holland.

Applications, giving full details of qualifications and experience, should be sent to:



**SHELL INTERNATIONAL
PETROLEUM COMPANY Ltd.,**

Recruitment Division (PNEL/31)

Shell Centre, London SE 1.

(1857)

SENIOR SCIENTIFIC OFFICER

required for

**Ministry of Agriculture, Fisheries and Food
Fisheries Experiment Station, Conway**

to investigate aspects of prawn culture in a re-circulation system. Duties include the study of nutritional requirements, the environmental and hormonal control of the breeding and moulting cycle and the operation of biological filters at elevated temperatures.

The appointment will be for a period of two years initially with possibility of a further year's extension, and would suit a biochemist, a physiologist, or a microbiologist.

QUALIFICATIONS: A good honours degree in a relevant scientific subject or an equivalent qualification, and at least four years' appropriate postgraduate or other approved experience.

AGE: At least 25 and normally under 32 years.

SALARY: £2,615 by 8 increments to £3,640 per annum. Short-term gratuity.

APPLICATION FORMS are available from Mr. N. J. L. Harris, Ministry of Agriculture, Fisheries and Food, Room 625, Great Westminster House, Horseferry Road, London SW1P 2AE. Telephone No. 01-834 8511, Ext. 7508 and 6245. Closing date for completed applications: December 31, 1973.

(1876)

DEAN, SCHOOL OF MEDICINE

**UNIVERSITY OF PENNA.
Philadelphia, Pa. U.S.A.**

Applications or nominations are sought for the position of Dean of the School of Medicine, University of Pennsylvania. Qualifications include an evidence of scholarship in the medical sciences and administrative experience in a biomedical institution or university. An M.D. degree is desirable, but not essential. Letters of inquiry, applications and nominations should be accompanied by a curriculum vitae. Direct communications through Dr. Howard Rasmussen, 403 Anatomy-Chemistry Bldg., School of Medicine-G3, University of Pennsylvania, Philadelphia, Pa. 19174 U.S.A.

An Equal Opportunity Employer.

(1909)

WESTERN AUSTRALIAN MUSEUM CURATOR OF FISH DIVISION OF NATURAL SCIENCE

Applications are invited for the above position. Qualifications: A degree in zoology with a higher degree in some aspect of ichthyology or a related field. Preference will be given to applicants with publications in taxonomy and with field experience.

Duties: As Curator of the Department of Fish, to be responsible to the Head of the Division of Natural Science for the development and care of the State collection of fish and research, the conduct of taxonomic research on the collections and the propagation of information about fish to the public. The appointee will be expected to develop a field-collecting programme embracing the marine and fresh water faunas of the State. He will advise and assist the Curator of Display to make displays within his field.

Salary: Curators are employed at Levels 3 and 4, Professional Division (Curatorial Officers), Salaries Agreement 1968. Present salary range Level 3 \$A8,826 to \$A9,708 (by 3 increments), Level 4 \$A9,986 to \$A11,396 (by 3 increments). The appointment will be made within Level 3, promotion to level 4 is consequent upon performance.

Conditions of Salary: Museum staff are employees of the Western Australian Museum under the Museum Act, 1969. Staff are entitled to the same leave and superannuation benefits as are Public Servants employed under the Public Service Act. Other conditions of service are fixed by the Trustees, but are similar to those applying in the public Service. All appointments are subject to confirmation after a probationary period of three months. Salary scales are fixed by arbitration.

Applications: Applications must include information as to nationality, date of birth, particulars of education and degrees. Applicants should also include the names of three referees competent to give information on professional ability and character. The successful applicant will be expected to provide evidence of good health before appointment. A recent photograph would be useful.

Information: Further information on duties and conditions of service may be obtained on application to the Director.

Closing date: Applications will close at Perth with the Director on January 31, 1974.

The Curator of Fish,
Western Australian Museum,
Perth, Western Australia 6000.

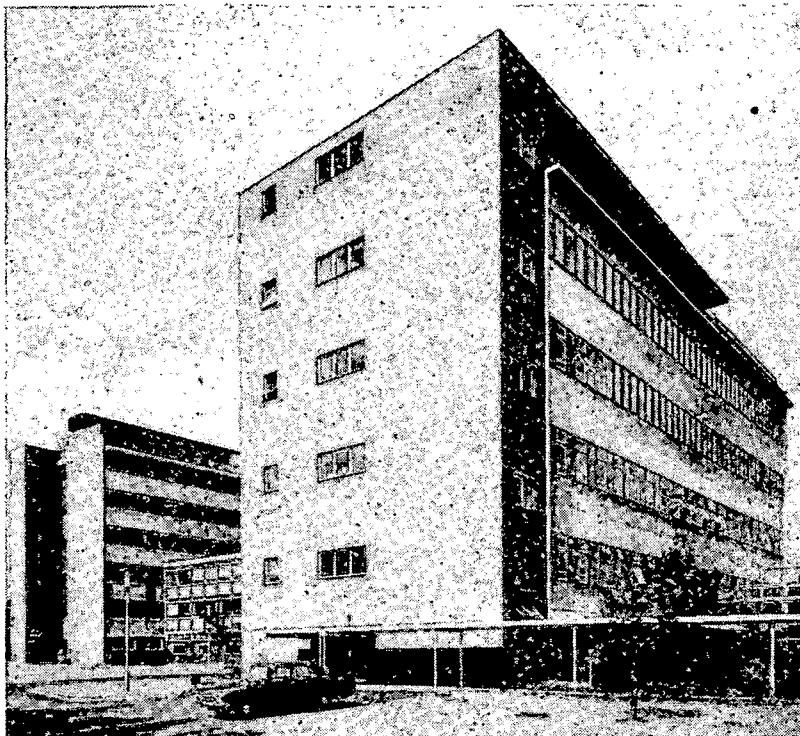
(1867)

UNIVERSITY OF OXFORD

There will be a vacancy for a POSTDOCTORAL BIOCHEMIST or MICROBIOLOGIST to work on bacterial sporulation. The appointment, which will be for one year in the first instance, at an initial stipend of £1,821, may be extended for a further period of two years and there is provision for F.S.S.U. or its equivalent.

Applications, which should include relevant details and the names of two referees, should be sent before February 1, 1974, to Professor J. Mandelstam, Microbiology Unit, Department of Biochemistry.

Analytical and Physical Chemists



May and Baker Ltd. invite applications for several posts in the Applied Physical Chemistry Division of the Research Institute at Dagenham. The appointments on offer would interest chemists wishing to be involved with environmental and/or metabolism studies in plants, animals, soil, water, etc., developing new methods of analysis or working on crystallisation phenomena. Extensive spectroscopic, radiochemical, electrochemical, chromatographic and other physical techniques are available for research and development studies on a wide range of fine chemicals for agricultural, industrial, medical and veterinary use.

May and Baker provide first-class conditions of employment including a highly competitive starting salary and contributory pension scheme with free life assurance cover. Assistance towards removal expenses may be considered in suitable cases.

Please apply in writing giving details of qualifications and experience to the Personnel Manager, May and Baker Ltd., Dagenham, Essex, RM10 7XS, quoting the reference number 309/N/1.

M&B May & Baker

(1859)



Appleton Laboratory, Sounding Rockets Division

Senior Scientific Officer/Professional and Technology Officer I

There is a vacancy at the Appleton Laboratory for a research officer to specify and keep under review the SRC's requirements on sounding rockets and their performance. These rockets carry experiments, in Astrophysics and Geophysics, supplied by University and Governmental Departments supported by the Science Research Council.

Duties To specify in collaboration with contractors and to keep under review such areas as aerodynamic design, flight characteristics, structural integrity, motor performance, rocket motor ignition switching, pyrotechnic devices and the design of parachute recovery systems for SRC purposes as outlined above. He will be required to supervise R & D in some of the above areas.

In addition, he will be expected to give advice on the design of balloon payload structures.

Qualifications and Experience

Applicants should be research orientated, preferably possessing an honours degree, equivalent membership of a professional institution or hold equivalent qualifications and have had experience in related areas to the duties described above.

Experience in some of the following areas of work is desirable: Rocket electrical, mechanical and pneumatic subsystems, payloads, data transmission and reduction, flight instrumentation such as rate gyros, accelerometers, attitude sensors, magnetometers, tracking beacons and telemetry systems.

Salary Scales: Senior Scientific Officer £2,615-£3,640

Professional and Technology Officer I £3,062-£3,923.

Non-contributory pension scheme.

Apply for an application form to:

The Secretary,
Science Research Council,
Appleton Laboratory,
Ditton Park, Slough SL3 9JX, Bucks.
Telephone: SLOUGH 44234

Closing Date: 17 December, 1973

(1893)



ANIMAL NUTRITION

In recent years ICI research in animal nutrition has increased rapidly. New products have been introduced to the market and others are at various stages of development. Both the commercial and research activity is expanding, leading to greater ICI business in these areas of agriculture both in the UK and Europe.

A Market-Oriented Nutritionist

is required by the New Business Opportunities Group at Billingham to join the team responsible for expanding the sales of existing forage preservation and animal nutrition products and for introducing new products to the UK and European markets.

The successful candidate is likely to be a graduate with a number of years of experience in the animal feedstuff industry, preferably with responsibilities in the technical service/market development areas and with an emphasis on ruminant nutrition.

He will be expected to work closely with research staff and complement their technical development work with commercial investigations on market planning and sales strategy. He must be capable of handling detailed discussions with the senior nutritionists in the animal feed industry, providing a technical service and advising agricultural sales staff in the field of animal nutrition.

This work, although based at Billingham, will involve travel both in the UK and abroad, particularly in Europe.

Write giving brief details of age, qualifications and experience to:
JHG Parfett, Personnel Department, Imperial Chemical Industries Limited,
Agricultural Division, PO Box 1, Billingham, Teesside TS23 1LB.

(1849)

Scientific Information

... an interesting field for a recently qualified graduate

The Science Information section of our Research & Development Services Division has a vacancy for a graduate in one of the biological sciences.

The main duties will be to carry out literature searches requested by members of the Biological and Medical Divisions, to prepare current awareness bulletins on selected topics of interest to research project groups, and to assist in operating internal information storage and retrieval systems. Previous experience of this type of work is not necessary, but the ability to write accurately and concisely is essential.

This is an exciting career opportunity in a growing and successful organisation. Our new laboratories are situated at Ware, a pleasant rural Hertfordshire town about 20 miles north of London. An excellent starting salary will be offered together with other attractive fringe benefits, including a share in the profitability of the Glaxo Group, of which we are a member. Assistance with relocation expenses will be given, where appropriate.



Please write giving brief relevant details of qualifications, experience and present salary to: G. R. Jones, Personnel Officer, Allen & Hanburys Research Ltd., Priory Street, Ware SG12 0DJ.



(1868)

UNIVERSITY OF STRATHCLYDE

DEPARTMENT OF PURE AND
APPLIED CHEMISTRY
(Polymer Physics Group)

POSTDOCTORAL RESEARCH ASSISTANT

Applications are invited for a Postdoctoral Research Assistantship in the Polymer Physics Group concerned with the experimental and theoretical study of molecular motion in polymer systems by relaxation techniques.

Candidates with a background in chemical engineering, chemistry, physics or applied mathematics will be considered.

The appointment will be on the salary scale £1,929-£2,058; placing dependent on qualifications and experience, and will be for one year in the first instance with the possibility of renewal for a further year. The appointment will be from January 1, 1974, or as soon as possible thereafter.

Applications (quoting R33/73) should be sent to Professor A. M. North, Department of Pure and Applied Chemistry, Thomas Graham Building, University of Strathclyde, 295 Cathedral Street, Glasgow, G1 1XL. (1830)

UNIVERSITY OF BRISTOL DEPARTMENT OF SURGERY

Applications are invited for the post of

RESEARCH ASSOCIATE/ASSISTANT

to study the immune responsiveness of patients with breast cancer. Candidates must possess a Ph.D. The post is annually renewable for two years from January 1, 1974, and carries a salary of up to £2,553 per annum. F.S.S.U. according to experience.

Applications in writing, with the names of two referees, to Dr. M. O. Symes, The Medical School, University Walk, Bristol BS8 1TD, by December 10, 1973, please. (1866)

MONASH UNIVERSITY AUSTRALIA

DEPARTMENT OF MECHANICAL
ENGINEERING

TEACHING FELLOW/SENIOR TEACHING FELLOW—HYDRAULICS/ FLUID MECHANICS

Major research facilities and courses of instruction in hydraulics and fluid mechanics for the Engineering Faculty are located in the Department. A good first degree or higher degree with an interest extending to civil engineering aspects of fluid mechanics is required.

Research interests include environmental flows; wind effects on buildings and structures; natural wind structure; density-stratified flows; fluid dynamics of estuaries and pollution studies. The latter include tides, turbulent diffusion and flushing of Westernport Bay.

Salary range: Teaching Fellow, \$A5,740 to \$A7,015; Senior Teaching Fellow, \$A7,270 to \$A8,698.

Benefits: Travelling expenses for appointee and family; removal allowance; repatriation after three years' appointment if desired; temporary housing for an initial period.

Further general information and details of application procedures are available from the Academic Registrar, Monash University, Wellington Road, Clayton, Victoria 3168, Australia, or the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF. Technical inquiries should be addressed to the Chairman, Professor R. G. Barden, in the University.

Closing date: 18 January 1974.

The University reserves the right to make no appointment or to appoint by invitation. (1913)

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS AL5 2JQ

ENTOMOLOGIST or PLANT PATHOLOGIST required by Plant Pathology Department for work on insect transmission of plant viruses. Minimum qualifications Pass Degree, H.N.C. or equivalent in biological subjects. Appointment in grade of Scientific Officer (£1,318 to £2,177). Starting salary will depend on qualifications and experience. Superannuation with non-pensionable allowance to off-set contributions. Further details on request.

Applications, naming two referees, to the Secretary by December 21, 1973, quoting Ref No. 1962

Toxicologist

Philips-Duphar is as a pharmaceutical-chemical industry part of the Philips group of companies.

In the Toxicological Department of Philips-Duphar a vacancy has arisen for a toxicologist with pharmacological and/or biochemical background.

We are looking for a person with experience in the toxicological evaluation of new compounds in the pharmaceutical industry.

His main responsibility will be the skilled evaluation of the results and the preparation of the reports of these experiments. Our laboratories are situated about 20 km from the centre of Amsterdam and it would be possible to live in an urban or rural environment according to preference. Assistance will be given, if needed, in finding accommodation.

In addition Dutch lessons will be provided for the successful applicant and his wife.

Fringe benefits and salary will compare favourably with similar positions in the industry.

Applicants should apply in writing Philips-Duphar B.V., Personnel Department, P.O. Box 2, Weesp, Holland.



PHILIPS-DUPHAR B.V., Pharmaceutisch-Chemische Industrie

(1902)

INSTITUTE OF OPHTHALMOLOGY (UNIVERSITY OF LONDON)

Judd Street, London, WC1H 9QS

A JUNIOR TECHNICIAN and a TECHNICIAN are required to assist in research on inflammatory and physiological processes in the eye.

Recent school leavers with good 'O' and/or 'A' level qualifications in English, mathematics and scientific subjects and an interest in a technical career are invited to apply for the junior post. Salary according to age: at age 18 £984 p.a., including London Weighting. Day release available.

Applicants for the Technician's post must have ONC, Ordinary IST, or equivalent qualifications and have had 2-3 years' experience in biochemical and/or pharmacological research in the Technician grade. Salary in the scale £1,566 to £2,318 p.a., including London Weighting, according to age and experience.

Applications to Professor E. S. Perkins at the above

A.R.C. PLANT GROWTH SUBSTANCE AND SYSTEMIC FUNGICIDE UNIT, WYE COLLEGE, (UNIVERSITY OF LONDON)

An officer is required to assist in studies on compounds which are physiologically active in plants. The work involves the synthesis of compounds and studies on their metabolism in plants.

Applicants should have a degree or equivalent qualification in chemistry and a particular interest in organic chemistry.

The appointment, which will be of three years' duration, will be in the Scientific Officer (£1,318 to £2,177 per annum) or Higher Scientific Officer (£2,076 to £2,667 per annum) grade according to qualifications and experience. A minimum of five years' post-qualifying experience is normally required for appointment in higher grade.

Further details from the Director, Systemic Fungicides Unit, Wye College, Ashford, Kent TN25 5AH, whom applications, naming two referees, should

UNIVERSITY OF LIVERPOOL SECOND CHAIR OF GEOLOGY

Applications are invited for the newly established Second Chair of Geology. The salary will be within the range approved for full-time professorial appointments, and in any case not less than £5,916 per annum.

Applications (12 copies), together with the names of three referees, should be received not later than January 10, 1974, by the undersigned, from whom further particulars may be obtained. (Candidates overseas may send one copy only by airmail.) Quote Ref. RV/N/80594.

H. H. BURCHNALL,
Registrar.

The University,
P.O. Box 147,
Liverpool L69 3GB

Director

Medical Research Council Demyelinating Diseases Unit

The Medical Research Council are seeking a Director for their Demyelinating Diseases Unit at Newcastle upon Tyne.

The Unit is situated within the grounds of the Newcastle General Hospital, close to the Regional Neurological Centre. It is at present engaged on a wide-ranging programme of research into the demyelinating diseases, particularly multiple sclerosis. It is hoped that work on these diseases will continue to form a significant part of the Unit's research. The Council are, however, anxious to maintain and develop their research effort in the general area of clinical neurology and the precise scope of the Unit's future programme would be a matter for discussion between the Director and the Council.

The person appointed as Director must have an established reputation as a scientific investigator in his own specialist field and evident ability to manage a research team. While he need not necessarily be medically qualified he will be expected to have a wide general interest in the application of fundamental research to clinical neurological problems and to establish collaborative links with clinicians in this field.

The Council attach great importance to maintaining and developing the Unit's association with relevant academic departments in the University of Newcastle upon Tyne, in particular the Department of Neurology, and with the clinical neurological department of the University Hospital Group. Arrangements for collaborative work with such departments will be a matter for negotiation between the Council and the University — with the participation of the Director and in the light of his research interests.

If the Director's work makes it possible for him to hold an honorary clinical contract and this is awarded at consultant level, he will be paid on the MRC clinical scale at a suitable point in the NHS consultant grade (maximum at present £7599 p.a.). If the holding of a clinical contract is not appropriate, the Director will be paid at MRC non-clinical rates at a suitable point in the range up to £7641 p.a. Superannuation provision under the Federated Superannuation Scheme for Universities.

Applications should be submitted not later than 21 January 1974 in the form of a statement of about 400 words outlining in general terms the scientific programme that the applicant would wish to undertake and indicating the type of staff and other facilities required, together with a *curriculum vitae* and list of publications, to the Secretary, Medical Research Council, 20 Park Crescent, London W1N 4AL. Further particulars may be obtained from Mr. P. G. Daly, at the same address (or telephone 01-636 5422 ext. 101).

MRC
Medical Research Council

(1878)

THE UNITED SHEFFIELD HOSPITALS

PRINCIPAL NON-MEDICAL SCIENTIFIC OFFICER

required to act as Deputy to the Director of the Protein Reference Unit (Supra-regional Laboratory for Specific Proteins) Department of Immunology.

Experience in the clinical applications of immunochemistry together with a sound basic knowledge of protein chemistry and immunochemical methods an advantage. For further details please contact Dr A. W. Ward. (Tel. 0742-26484, ext. 229.)

Whitley Council Terms and Conditions of Service apply.

Salary £3,708-£4,836 p.a.

Applications, giving details of age, qualifications, experience, and the names and addresses of 2 referees, to The Acting Chief Administrative Officer, United Sheffield Hospitals, 10 Beech Hill Road, Sheffield S10 2RZ, by December 22, 1973. (1883)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF CANCER STUDIES

RESEARCH FELLOW

This is a vacancy for a research fellow/associate to carry out a study on the properties of cells derived from tissues treated with carcinogenic agents. The work would involve both tissue culture studies and animal experimentation. The fellowship is supported by the Cancer Research Campaign. Candidates should preferably be postdoctoral but a candidate with a good degree in biological science and experience in the appropriate area would be considered. Salary will be on the scale £1,929-£2,223 for a fellow and £1,569-£2,223 for an associate.

Applications, with curriculum vitae and names of two academic referees, should be sent to Professor D. G. Harnden, Department of Cancer Studies, Medical School, Birmingham B15 2TJ before January 4, 1974. (1921)

UNIVERSITY OF SHEFFIELD

TECHNICIAN (GRADE 4)

required for the Department of Biochemistry to assist in biochemical research. An interest in kinetics would be an advantage. Salary scale £1,848 by £63 (5) to £2,163 per annum. The working conditions and surroundings are pleasant; 37½-hour 5-day week with excellent holidays and other conditions of service. Please write to the Deputy Director of Services (Ref. B61/0), The University, Sheffield S10 2TN. (1846)

THE UNIVERSITY OF SHEFFIELD EXPERIMENTAL OFFICER

Applications are invited for a post of Experimental Officer to operate and maintain a Fourier-Transform N.M.R. Spectrometer in the Department of Chemistry. The successful applicant, who should be a graduate or have an equivalent professional qualification, will be responsible for operating a service in connection with a number of research projects in inorganic, organic, and physical chemistry. Previous experience in one or more of the following fields would be an advantage, although not essential: N.M.R. spectrometry, chemical instrumentation, electronics, and computing. The post is financed by the Science Research Council and the starting salary will be in the range £1,596 to £2,088 plus superannuation benefit.

Applications, including details of previous experience and the names of two referees, should be sent to Professor P. M. Maitlis, Department of Chemistry, The University, Sheffield S3 7HF, from whom further particulars may also be obtained. (Quote Ref. R4/G. (1895))

UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF METALLURGY AND
MATERIALS SCIENCE

SECRETARY OF THE DEPARTMENT OF METALLURGY AND MATERIALS SCIENCE

Applications are invited for the post of Secretary to the Department of Metallurgy and Materials Science. The main duties will be to assist in the general administration of the Department including academic business, finance, research contracts and equipment.

Salary will be in the range £2,553 to £3,708.

Written applications, giving details of qualifications and experience, including the names and addresses of two referees, should be sent to Professor R. W. K. Honeycombe, Department of Metallurgy and Materials Science, Pembroke Street, Cambridge CB2 3QZ, not later than December 21, 1973. (1895)

UNIVERSITY OF ALBERTA

Applications for GRADUATE STUDIES IN PHARMACOLOGY for the degrees of M.Sc. and Ph.D. are invited from students with a background in Biochemistry, Pharmacy, Biology, Chemistry or Medicine. Opportunities exist in Biochemical Pharmacology, Neuropharmacology and Smooth Muscle Pharmacology. Successful applicants may be eligible for financial assistance.

For further information write to: Dr I. S. Char-nock, Chairman, Department of Pharmacology, University of Alberta, Edmonton, Alberta, Canada, T6G 2H7. (1894)

Pathologist

Philips-Duphar is as a pharmaceutical-chemical industry part of the Philips group of companies.

In the Toxicological Department of Philips-Duphar a vacancy for a pathologist has arisen. We are looking for a person experienced in animal pathology.

The successful applicant will be involved in the experimental design of experiments out by or on behalf of the Department during the development of new drugs, pesticides, fine chemicals, etc. His main responsibility will be the skilled pathological evaluation of the results and the preparation of the reports of these experiments.

Our laboratories are situated about 20 km from the centre of Amsterdam and it would be possible to live in an urban or rural environment according to preference. Assistance will be given, if needed, in finding accommodation.

In addition Dutch lessons will be provided for the successful applicant and his wife.

Fringe benefits and salary will compare favourably with similar positions in the industry.

Applicants should apply in writing Philips-Duphar B.V., Personnel Department, P.O. Box 2, Weesp, Holland.



PHILIPS-DUPHAR B.V., Pharmaceutisch-Chemische Industrie

(1901)

INSTITUTE OF OPHTHALMOLOGY (UNIVERSITY OF LONDON) Judd Street, London, WC1H 9QS

A vacancy exists for a young IMMUNOLOGIST, preferably post-doctoral, with experience in cell-mediated immunity, to join a project of research on the role of cell-mediated immune mechanisms in human chlamydial disease. This work is associated with clinical and laboratory projects on ocular and genital chlamydial disease in London and hyperendemic trachoma in Iran. The appointment will be for three years in the first instance. Commencing salary £2,058 plus £162 London Allowance.

Applications, with full details of qualifications and experience, together with names and addresses of two referees, to The Secretary at the above address by December 15, 1973. (1882)

UNIVERSITY OF MANCHESTER RESEARCH BIOCHEMIST

Applications invited from biochemists with post-graduate experience, preferably in immunochemistry or the biochemistry of peptides, for the post of Biochemical Research Assistant in the Metabolic Division of the Department of Medicine. This post is available up to April 1978. The appointee would join a group engaged in research on parathyroid hormone, its radioimmunoassay, the separation and immunochemical identification of polypeptide hormonal secretion by parathyroid glands in organ culture. Salary range per annum: £1,716 to £2,223.

Further particulars and application forms (returnable by December 22) from the Registrar, The University, Manchester M13 9PL. Quote ref.: 215/73/N. (1839)

UNIVERSITY OF READING DEPARTMENT OF MICROBIOLOGY RESEARCH DEMONSTRATOR

Applicants should be graduates in Microbiology with a main interest in bacteriology. The appointment is for 3 years and carries a salary of £1,047×51 to £1,149 p.a. The Demonstrator is expected to assist in the practical class up to a maximum of 8 hours per week during term and to engage in research leading to a higher degree.

Applications, together with curriculum vitae and the names of 2 referees, should be sent to Dr R. M. Keddie, Department of Microbiology, University of Reading, London Road, Reading RG1 5AQ. (Ref. TN 50.) (1886)

TECHNICAL RESEARCH ASSISTANT

Fisons Limited, Pharmaceutical Division have a vacancy at their Research and Development Laboratories at Loughborough for a Technical Research Assistant to work in the Allergy Section of their Pharmacology and Biochemistry Department.

Applicants should preferably possess H.N.C. or equivalent qualifications in Pharmacology or related subjects. Experience of work in an industrial laboratory would be an advantage. We are a member of the Fisons Group, providing a first class pensions scheme, generous holidays, assistance with removal expenses where appropriate and other welfare benefits which come from being part of a large internationally known British Group.

Please write quoting Job Reference No. 246R to: Research Personnel Assistant, Fisons Limited, Research & Development Laboratories, Bakewell Road,

Loughborough,
Leicestershire.



(1880)

Glaxo

TECHNICIAN— Microbiology Department

A young Technician is required in our Research Laboratories at Greenford, Middlesex. The post is likely to appeal to people working for or who have recently gained HNC or similar qualifications.

A major part of the work will be evaluating new antimicrobial agents in animals. Previous experience of animal work would be an advantage.

Conditions of employment are attractive and include pension and bonus schemes. Flexible working hours are to be introduced shortly.



Please apply with full personal details to:
Personnel Officer (Research) Glaxo Laboratories Ltd.,
Greenford, Middlesex, quoting ref. No. 672.

(1897)

THE INTERNATIONAL LABORATORY OF MARINE RADIOACTIVITY OF THE INTERNATIONAL ATOMIC ENERGY AGENCY in MONACO has an opening at the **Assistant Officer's** level. The successful candidate should have knowledge and some experience in marine radioecological research and related techniques. Experience in studying the effects of stresses on marine organisms is desirable. Ph.D. or equivalent in biological oceanography or marine radioecology necessary.

Emoluments US\$10,282 per annum if single, additional benefits if married. Travel and removal expenses paid.

Send curriculum vitae to Division of Personnel, International Atomic Energy Agency, P.O. Box 590, A-1011 Vienna, Austria, not later than ten days from today.

(1850)

SENIOR HARVARD CHAIR in the School of Public Health, the John Rock Professor of Population Sciences is to be filled by a scholar specialising in population. Harvard is an equal opportunity employer.—To be considered please write Dr Howard H. Hiatt, Dean, Harvard School of Public Health, 55 Shattuck Street, Boston, Massachusetts 02115. (1918)

APPLICATIONS ARE INVITED for a position at the Assistant Professor level in the field of cell biology.—Résumés, with references and reprints, should be sent to Dr A. H. Houston, Professor and Chairman, Department of Biological Sciences, Brock University, St Catharines, Ontario.

UNIVERSITY OF OXFORD UNIVERSITY LECTURESHIP IN ANATOMY

The University proposes to appoint a Lecturer in Anatomy. Applications are especially invited from candidates whose research interests lie in the fields of developmental and cell biology, experimental neurology, or endocrinology. The salary will be according to age on the scale £1,929 to £4,863. The person appointed will be required to pay contributions to a superannuation scheme as prescribed by the Statutes and Decrees of the University. At present, staff of academic or equivalent status are required to belong to F.S.S.U., but it is possible that other arrangements will be introduced. The successful candidate, if a man, may also hold a Fellowship at Magdalen College. The attention of candidates is drawn to the accompanying advertisement by Magdalen College.

Applications (5 copies), with curriculum vitae and the names of referees, should be sent to Professor A. G. M. Weddell, Department of Human Anatomy, South Parks Road, Oxford OX1 3QX, not later than January 2, 1974. (1861)

MAGDALEN COLLEGE, OXFORD FELLOWSHIP IN ANATOMY

The College proposes to elect a Fellow and Tutor in Anatomy. A university Lectureship in Anatomy may be associated with this Fellowship, and attention is drawn to the advertisement for this post. The Fellow will be expected to tutor undergraduates reading Medicine and Physiological Sciences, for which he will receive additional stipends. He will be entitled to free rooms in College or a housing allowance if married.

Further particulars can be obtained from the President, Magdalen College, to whom applications should be submitted by January 22, 1974. (1862)

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG, SOUTH AFRICA NUCLEAR PHYSICS RESEARCH UNIT ACCELERATOR PHYSICIST

NUCLEAR STRUCTURE GROUP ON THE
GRADE OF SENIOR RESEARCH OFFICER

Applications are invited from suitably qualified persons for appointment to the above post. Duties are to be assumed as soon as possible. The incumbent will be expected to participate in the Nuclear Structure Research projects of the Unit and may be required to contribute to the development, maintenance and use of accelerator facilities. The present facilities include an EN Tandem van de Graaff accelerator and a 2 MeV pressurised Cockcroft-Walton set.

The salary will be in the range R7,245 to R9,315 (R1=60p approximately); the initial salary to be determined according to qualifications and experience. Benefits include an annual bonus, pension, and medical aid facilities, and a housing subsidy (if eligible).

Intending applicants should obtain the information sheet relating to the post from the Registrar, University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, South Africa, with whom applications should be lodged not later than January 31, 1974. Copies of the information sheet may also be obtained from the London Representative, University of the Witwatersrand, Chichester House, 78 High Holborn, London WC1, to whom a copy of the application should be sent. (1875)

UNIVERSITY OF GUELPH ZOOLOGISTS (5 POSITIONS)

Applications are invited from suitably qualified persons to teach undergraduate courses, as required, on one or more of the following: introductory biology, invertebrate zoology, limnology, physiology, ecology, developmental biology and histology, and wildlife biology (some management experience would be useful). The department supports strong undergraduate and graduate programmes in fisheries and wildlife biology, marine biology, physiology, ecology, parasitology and animal behaviour. The present positions offer excellent opportunities to develop additional programmes in areas of the applicants' interests. Salary and position will be at a level commensurate with experience. Some appointments may be made immediately.

Applications must include the names of two referees and should be forwarded to the Chairman, Department of Zoology, College of Biological Science, University of Guelph, Guelph, Ontario, Canada N1G 2W1, by February 28, 1974. (1908)

PORTSMOUTH POLYTECHNIC

DEPARTMENT OF MATHEMATICS

RESEARCH ASSISTANTSHIP IN SIGNAL ANALYSIS AND PROCESSING

Applications for the above post are invited from first or second class honours graduates in Mathematics, Science or Engineering, with a special interest in Stochastic Processes and/or signal analysis. The successful candidate will be expected to work for a higher degree and will be encouraged to publish his results.

Salary scale: £1,230 to £1,330 per annum.

Application forms and further particulars may be obtained from Dr J. Hammond, Department of Mathematics, Portsmouth Polytechnic, Hampshire Terrace, Portsmouth PO1 2EG, to whom completed applications should be returned by December 17, 1973. Please quote reference M7. (1832)

AVON AND DORSET RIVER AUTHORITY BIOLOGIST

Applications are invited from young graduates for the temporary post of Biologist. The successful applicant will be given a 3 year contract within the A.P. Grades 2-3 (£1,644-£2,535), to investigate particular aspects of the ecology of the River Frome (Dorset). Salary within the above grades according to qualifications and experience.

Full particulars and application form may be obtained from: The Fisheries and Pollution Officer, Avon and Dorset River Authority, County Gates House, 300 Poole Road, Parkstone, Poole, Dorset, BH12 1AU.

Closing date for completed applications: December 28, 1973. (1920)

UNIVERSITY OF ABERDEEN RESEARCH ASSISTANT IN BIOCHEMISTRY

Applications are invited for above post to work under the supervision of Dr. I. P. Williamson on the effects of methylmalonate on fatty acid biosynthesis. Salary within range £1,479 to £1,659.

Further particulars from the Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by December 20, 1973. (1874)

ROYAL POSTGRADUATE MEDICAL SCHOOL

GRADUATE SCIENTIFIC OFFICER

required to work in the field of Immuno-Stimulation. Candidates should hold a degree in biochemistry, biology, zoology or some related subject, and previous experience in cellular immunology an advantage. Starting salary according to qualifications and experience, but no less than £1,812 per annum.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting Reference 3/229/N. (1900)

The University of Leeds DEPARTMENT OF PURE AND APPLIED ZOOLOGY

Applications are invited for a post of RESEARCH ASSISTANT to assist in an investigation of the population ecology of 'fungus feeding' species of *Drosophila*. Possession of a driving licence would be an advantage. Salary scale £1,449-£1,692.

Forms of application and further particulars from the Registrar, The University, Leeds LS2 9JT (please quote 26/8/D). Closing date December 21, 1973. (1889)

CLINICAL RESEARCH ASSOCIATE

c. £3,000

Stoke Poges, Buckinghamshire

We have created a new position in our Scientific and Medical Division for a Clinical Research Associate who will need to hold a degree or equivalent (eg: FIMLT) in Biological Sciences and, ideally, have some hospital laboratory work experience.

The job will involve planning and implementation of new product field trials of AMES COMPANY, including selection and briefing of investigators and the briefing and training of marketing staff prior to product launch. A contribution to the identification of potential new products will be expected, as well as the planning and implementation of utility trials and the application of experience gained from product trials to marketing needs and to technical field enquiries.

Accountable directly to our Medical Director the job will involve a good deal of travelling and a company car will be provided. Company benefits include four weeks annual holiday, free life insurance and contributory pension scheme. Attractive country location.

Please write or telephone
Mrs Nancy Morgans,
Personnel Manager,
Farnham Common (02814)
2151, for an application form
and job description.
Miles Laboratories Limited,
Stoke Court, Stoke Poges,
SLOUGH SL2 4LY, Bucks.

(1896)

MILES

Exploration with TOTAL Geophysicist

London

TOTAL OIL MARINE, the exploration subsidiary of one of the oil majors, is rapidly expanding its activities in the North Sea and invites applications for the position of Geophysicist to augment its exploration staff.

Reporting directly to our Senior Geophysicist his duties will principally be geophysical interpretation of seismic data. Activities may also involve quality control of the acquisition and processing of this data.

He should have a sound and practically orientated geological background together with about 5 years' relevant experience preferably in the North Sea. He will probably be about 30. A knowledge of French would be desirable.

Salary will be competitively negotiable dependent upon experience. Benefits include pension, life insurance and assistance with relocation where appropriate.

Applications to: N. V. HOLT, TOTAL OIL MARINE, GLEN HOUSE, STAG PLACE, LONDON SW1 5AY. TELEPHONE 01-834 3436.

(1915)

University of Zambia

The University of Zambia is seeking staff for the academic year 1974/75 (which begins in June 1974) in the subjects detailed below:

1. **PROFESSOR/SENIOR LECTURER IN FARM MECHANISATION IN THE SCHOOL OF AGRICULTURAL SCIENCES.** Applicants should hold an M.Sc. or Ph.D., have extensive teaching experience at university level, extensive research experience preferably relating to problems of tropical agriculture and have experience in academic administration and extra-curricular activities. Appointee will be expected to teach farm mechanisation to undergraduates and to assist in the design of the Department's teaching and research facilities.

2. **PROFESSOR/SENIOR LECTURER/LECTURER IN GEOGRAPHY.** Experience in Physical Geography and/or Geomorphology will be an advantage.

3. **READER/SENIOR LECTURER/LECTURER IN CHEMISTRY.** Experience in Analytical, Inorganic, Organic and Physical Chemistry is essential. One appointee is required specifically for teaching First Year General Chemistry.

4. **SENIOR LECTURER/LECTURER/ASSISTANT LECTURER IN PHYSICS.** Duties will include first year teaching and laboratory demonstrating and to assist the Head of subject in the general administration and development of the subject.

Salary scales: Professor K7,400 to K7,800 per annum. Reader £6,800 per annum. Senior Lecturer K5,600 to K6,600 per annum. Lecturer K4,000 to K5,400 per annum. Assistant Lecturer K3,200 to K3,800 per annum (£1 sterling=K1.53). The British Government may supplement salaries of Professor, Reader, Senior Lecturer and Lecturer in range £200 to £750 per annum (sterling) for married appointees of £100 to £350 per annum (sterling) for single appointees (normally free of all tax) and provide children's education allowances and holiday visit passages. This supplementation is unlikely to be applied to appointments at Assistant Lecturer level. Family passages; various allowances; superannuation and medical aid schemes; regular overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail, not later than January 3, 1974 to the Registrar, University of Zambia, P.O. Box 2379, Lusaka, Zambia. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address.

(1842)

DEPARTMENT OF CYTOGENETICS THE CHARLES HAYWARD RESEARCH BUILDING QUEEN ELIZABETH HOSPITAL FOR CHILDREN Hackney Road, London, E2 8PS

TECHNICIAN or JUNIOR TECHNICIAN

required in the above department for routine diagnostic and research laboratory work concerned with the investigation of human chromosome abnormalities including antenatal studies. Specific experience not essential as training will be given. Whitley Council salary and conditions of service. Minimum qualifications—2 science 'A' levels or O.N.C. Graduates in the biological sciences with ordinary degrees who are or intend to become State Registered technicians will be considered.

Write, giving personal details, curriculum vitae and the names of two referees to the Senior Cytogeneticist from whom further information can be obtained.

(1854)

The University of Leeds DEPARTMENT OF PLANT SCIENCES

Applications are invited for the post of **RESEARCH ASSISTANT** to work with Dr L. V. Evans on physiological/structural aspects of host-epiphyte relationships in seaweeds. Experience of current biochemical techniques an advantage. The appointment will be for one year in the first instance, renewable for a further period of two years, and is financed by NERC. Salary £1,449-£1,692.

Forms of application and further particulars from the Registrar, The University, Leeds LS2 9JT (please quote 41A/8/D). Applications should be received as soon as possible. (1922)

UNIVERSITY OF SHEFFIELD DEPARTMENT OF METALLURGY POSTDOCTORAL RESEARCH ASSISTANT FOR HOT WORKING RESEARCH

Applications are invited for a post of **RESEARCH ASSISTANT** to work on the metallurgy of hot working operations. The research, which is supported by a grant from the Science Research Council, would involve study of the evolution of flow stress and structure during interrupted deformation sequences carried out on a computer controlled servo-hydraulic testing machine to simulate hot rolling of forging operations. The appointment is tenable from January 1, 1974, or a date to be arranged to December 31, 1976, with an initial salary of up to £2,058 rising to £2,388. Previous experience in hot working research is desirable but not essential. Further particulars from the Registrar and Secretary, The University, Sheffield S10 2TN, to whom applications, including a brief curriculum vitae, research experience, and the names and addresses of two referees, should be sent as soon as possible. Please quote R2/G. (1848)

CULTURE CENTRE OF ALGAE AND PROTOZOA CAMBRIDGE

Preservation of Living Cultures

The Culture Centre of Algae and Protozoa intends appointing a Scientist (HSO/SSO) to initiate and carry out a programme of long-term preservation of cultures of algae and free-living protozoa. The person appointed should have experience in the freezing or freeze-drying of organisms or tissues and sufficient knowledge of cryobiology and cell biology to be able to develop new techniques where necessary.

Qualifications: A good honours degree or equivalent qualification and at least two years' postgraduate training or experience related to the preservation of organisms or biological material. Experience with algae and protozoa is not essential.

Salary scales:

Higher Scientific Officer, £2,076 to £2,667.

Senior Scientific Officer, £2,615 to £3,640.

Starting salary may be above the minimum.

Superannuation arrangements.

Application form and further particulars from the Director, Culture Centre of Algae and Protozoa, 36 Storey's Way, Cambridge CB3 0DT.

Closing date: December 31, 1973.

NATURAL ENVIRONMENT RESEARCH COUNCIL

(1844)

PHYSICIST REQUIRED FOR VACANCY in small M.R.C. team working on the development and behaviour of the avian embryo, including its capacity to receive and transmit signals. We want a research worker who will make use of his basic knowledge to help solve our problems. Some aptitude for electronics essential. Medical Research Council scales. F.S.S.U.—Inquiries to Margaret A. Vince, Psychological Laboratory, Downing Street, Cambridge CB2 3EB. (1856)

JUNIOR TECHNICIAN required to join group in the Department of Clinical Pharmacology monitoring concentrations of drugs in plasma. Experience of thin layer and gas chromatography an advantage but not essential.

Minimum qualifications: G.C.E. 'O' level passes in English, Mathematics and two science subjects. Salary according to qualifications and experience. Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, Duane Road, London W12 0HS, quoting Ref. 20/476N. (1914)

UNIVERSITY OF CALGARY

Applications are invited from students wishing to conduct **GRADUATE STUDIES IN BIOLOGICAL SCIENCES** for the Ph.D. or M.Sc. degree. Successful applicants may compete for Teaching and Research Assistantships which carry a stipend, remission of fees and a travel allowance.

For further information write to: The Secretary for Graduate Studies, Department of Biology, University of Calgary, Calgary T2N 1N4.

UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF BOTANY

Applications are invited from suitably qualified PLANT PATHOLOGISTS for appointment as UNIVERSITY LECTURER.

Applications (10 copies), with names of three referees, should be sent by January 21, 1974, to Secretary, Appointments Committee, Faculty of Biology A, Department of Applied Biology, Downing Street, Cambridge CB2 3DX, from whom further particulars may be obtained. (1871)

A NEW MEDICAL SCHOOL

AT MEMORIAL UNIVERSITY OF
NEWFOUNDLAND, ST. JOHN'S,
NEWFOUNDLAND, CANADA

is expanding its faculty and is now ready to make appointments in the field of cell sciences. New buildings to house the cell sciences research group, which is part of the larger division of cell studies, will be ready for occupancy by 1975. The health sciences complex now under construction is a medical school with extensive research areas plus a biomedical library and 400-bed hospital.

Applications are now invited for a senior level position who would be able to organize a research team and participate in the inter-disciplinary teaching of medical students.

Interested individuals should submit applications, accompanied by a detailed curriculum vitae, to Professor B. H. Sells, Ph.D., Chairman, Search Committee, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland, Canada. (1910)

UNIVERSITY OF
NEWCASTLE UPON TYNE
TWO LECTURESHIPS
IN PSYCHOLOGY

Applications are invited for two Lectureships in the Department of Psychology. The department is mainly looking for candidates whose chief interests are in the fields of Personality or Mathematical and Statistical Psychology; but suitable persons in other areas should not be dissuaded from applying.

Salary will be at an appropriate point on the Lecturers' scale, £1,929 to £4,548 according to age, qualifications and experience. Membership of F.S.S.U. required.

Further particulars may be obtained from the Registrar, The University, Newcastle upon Tyne NE1 7RU with whom applications (3 copies), together with the names and addresses of three referees, should be lodged not later than January 31, 1974. Please quote reference N. (1838)

UNIVERSITY OF MELBOURNE
LECTURESHIP
in the
DEPARTMENT OF GENETICS

Preference will be given to an applicant in the field of biochemical and developmental genetics of eukaryotes. Excellent facilities for this type of work (including an Electron Microscope) are available in the Department. The Department of Genetics (Head, Professor M. J. D. White, F.R.S.) has an academic staff of seven.

The successful applicant will be expected to commence duties as early as possible in 1974.

Salary: \$A8,698-\$11,982.

Further information, including conditions of appointment and method of application, is available from the Association of Commonwealth Universities (Apts.), 36 Gorden Square, London WC1H 0PF. Applications close of February 15, 1974. (1923)

MACQUARIE UNIVERSITY
SYDNEY, AUSTRALIA
SENIOR LECTURER/LECTURER
IN BIOLOGY

Applications are invited for the above-mentioned appointment in the School of Biological Sciences. The appointee will be required to teach courses in plant physiology and should have experience in the sphere of whole-plant and/or environmental physiology.

It is hoped that the appointee will be able to take up duty by July 1, 1974, in time for the commencement of teaching for the second half year.

Salaries will be within the ranges \$A12,268 with five annual increments to \$A14,308 per annum for a Senior Lecturer and \$A8,698 with seven annual increments to \$11,982 per annum for a Lecturer.

Further information about the University and advice regarding the method of application should be obtained from the Secretary-General, Association of Commonwealth Universities (Apts.), 36 Gorden Square, London WC1H 0PF, or from the Registrar, Macquarie University, North Ryde, N.S.W. 2113, Australia.

Applications close on January 25, 1974. (1925)

SCIENTIFIC RESEARCH COUNCIL
JAMAICA, W. I.

Scientific Officer

Applications for the post of Scientific Officer in the Mineral Resources Division are invited from suitably qualified persons. The minimum qualifications for the post are:-

1. A good degree in Chemical Engineering.
2. Drive, initiative and an interest in research and development. Postgraduate experience either in Industry or in University will be an asset.

Duties will include participation in the Council's projects at the pilot plant stage. Priority attention will be devoted to the processing technology of bauxite.

Salary will be in the range J\$3,480-J\$6,960; the point of entry depending on qualifications and experience.

The Council provides Superannuation, Life and Health Insurance Schemes.

Applications stating age and full details of qualifications and experience together with the names and addresses of three referees should reach the Technical Director, Scientific Research Council, P.O. Box 502, Kingston, Jamaica, W.I. not later than Monday, 31st December, 1973. (1916)

EUROPEAN ORGANIZATION FOR RESEARCH ON TREATMENT OF CANCER
(E.O.R.T.C.)

Institut Jules Bordet, Brussels

2 BIOSTATISTICIANS

E.O.R.T.C. is seeking 2 biostatisticians (Doctorate and Master level) interested in cooperative clinical trials in cancer. Their task will be to advise on protocol design, to follow-up on-going studies, to assume quality control and to perform data analysis for the new therapies of cancer, and in general to deal with all aspects of statistics as applied to clinical and experimental medicine. They will also be expected to carry out their own research. There exists excellent facilities at the Brussels University for such type of work: libraries, computer centre, etc.

Knowledge of another European language is an asset but not essential.

Salaries will vary according to experience.

Write with curriculum vitae and references to: Dr. M. Staquet, Institut Jules Bordet, 1 rue Héger-Bordet, 1000 Brussels, Belgium. Tel. (02) 38 57 90. (1887)

THE INTERNATIONAL LABORATORY OF MARINE RADIOACTIVITY OF THE INTERNATIONAL ATOMIC ENERGY AGENCY in MONACO has an opening at the P2/P3 level. The successful candidate should have a comprehensive knowledge and experience in the analytical techniques of gas chromatography. In addition, a background in organic analytical chemistry is desirable. Ph.D. in chemistry or chemical oceanography necessary. Two to six years' experience.

Emoluments in the region of US\$13,000 to US\$18,000 depending on experience and qualifications. Travel and removal expenses paid. Allowances for dependent spouse and children.

Send curriculum vitae to Division of Personnel, International Atomic Energy Agency, P.O. Box 590, A-1011 Vienna, Austria, not later than ten days from today. (1851)

NEW LEICESTERSHIRE COUNTY COUNCIL
MUSEUMS, ART GALLERIES & RECORDS SERVICE

TECHNICIAN, GEOLOGY

We are looking for a technician to be responsible to the Keeper of Geology for providing technical and conservation support to the Geology Section. Work will include the cleaning, repair and development of geological specimens, the management of a small geological laboratory, and assisting with geological collecting, recording and other fieldwork throughout the County.

Applicants should be experienced laboratory technicians, preferably with experience in geological preparation work. However, those without geological experience but with an adequate educational background (with a minimum of A levels in chemistry and geology) and a willingness to learn, will be considered.

Salary: T3-4 (£1,416-£1,926) the starting salary depending on qualifications and experience. For further details and an application form please write or telephone The Director of Museums and Art Galleries, New Walk, Leicester LE1 6TD (Tel. no. 26832).

Closing date for completed application forms, December 19, 1973. (1864)

TECHNICIAN

(qualified) required for work in immunology in relation to renal disease. Experience in this field is not essential.

Apply in writing, stating age and giving details of education and experience, to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, quoting Ref. R.U.1. (1877)

**UNIVERSITY COLLEGE OF WALES
ABERYSTWYTH**

DEPARTMENT OF AGRICULTURE

Applications are invited for the post of **LECTURER** in Agriculture to commence in October 1974. Salary on a scale £1,929 to £4,548 per annum.

Application forms and further particulars may be obtained from the Registrar, to whom applications should be sent by December 31, 1973. (1860)

ASSISTANTS AND FELLOWSHIPS

available for graduate study in materials science and engineering leading to M.Sc. and Ph.D. Research areas include mechanical properties, crystal growth, surfaces, corrosion, electronic properties, biomaterials, fuel cells and batteries, phase transformations and materials synthesis and processing.

For information write: Chairman, Department of Materials Science and Engineering, Stanford University, Stanford, California 94305. (1912)

UNIVERSITY OF CALGARY, GRADUATE Teaching and Research Assistantships are available for students proceeding to the Ph.D. or M.Sc. degrees in all branches of Chemistry and Biochemistry. The Assistantships are valued from \$4,100 to \$5,000 per annum and carry remission of programme fees and travel allowance.

For further information write to: Department of Chemistry, Calgary, Alberta T2N 1N4, Canada. Please indicate field of interest. (1903)

TECHNICIAN GRADE 3 REQUIRED to assist in a research programme under the direction of Professor B. R. Rabin. The post is supported by a project grant from the M.R.C. The work is in the field of chemical carcinogenesis and involves studies of intracellular membranes, protein synthesis and steroid hormone action. Salary in range £1,650 to £1,920 plus £175 London Weighting.—Application form from Personnel Officer (Technical Staff FC9), University College London, Gower Street, London WC1E 6BT. (1841)

ANALYTICAL CHEMIST required with experience in elemental analysis (CHN etc.). Other experience useful.—Write with full details, Maybridge Chemical Co. Ltd., Tintagel, N. Cornwall, U.K. (1892)

TECHNICIAN required in Department of Zoology, University of Reading, to be responsible for day to day running of the electron microscopy laboratories. Qualifications should include recent experience of electron microscope maintenance. Some preparative techniques for biological material is desirable. Salary in scale £2,007-£2,382 p.a. (Grade 5).—Apply for further particulars, quoting Ref. TN80, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH. (1885)

**FELLOWSHIPS AND
STUDENTSHIPS**

**UNIVERSITY OF OXFORD
THE QUEEN'S COLLEGE
BROWNE RESEARCH FELLOWSHIP**

The Governing Body proposes, if a suitable candidate presents himself, to elect a Brown Research Fellow in Botany or Zoology. The choice of the College will not be limited to candidates intending to work in the Departments of Botany or Zoology. The successful candidate will enter upon his Fellowship on October 1, 1974.

The Fellowship is of the value of £1,560 per annum and is pensionable under the Federated Superannuation System for Universities. It will be tenable for three years and may (but only in exceptional circumstances) be renewed for a further period not exceeding two years. The Fellow will be entitled to free rooms in College (or in approved cases to an increase of stipend in lieu) and to free lunch and dinner at the common table. A Browne Research Fellow may, with the leave of the Governing Body, engage in teaching up to a maximum of six hours weekly.

Candidates must be graduates of an approved University, and must not have exceeded thirty terms from their matriculation by October 1, 1974. Candidates should apply to The Provost, The Queen's College, Oxford, not later than January 14, 1974, stating their qualifications, including any research in which they have been engaged, and the names of three persons prepared to act as referees. (1919)



**RESERVE BANK OF
AUSTRALIA
SENIOR RESEARCH
FELLOWSHIPS
(AGRICULTURE)**

The Reserve Bank of Australia invites applications for Senior Research Fellowships for applied research in agriculture. The research to be undertaken may be in any of the broad fields of economics and management, plant sciences or animal sciences. The awards are not primarily intended to provide opportunities to obtain higher degrees or to obtain immediate postdoctoral research experience.

The Fellowships will be initially for two years with the possibility of extension for a further year and will be tenable at an Australian university or other approved Australian scientific research institution. Candidates should be in a position to take up the awards no later than July, 1975.

The award of the Fellowships will be made by the Reserve Bank of Australia on the advice of a Selection Committee including scientists, representatives of universities and other research institutions. The final decision as to the nature of the research to be undertaken and the place of tenure will be made by the Reserve Bank of Australia after consultation with the successful candidates and the host research institution. It is planned to announce the names of the successful candidates in late September or early October, 1974.

The Fellowships are intended to foster closer liaison between agricultural research institutions in Australia; to provide an incentive for experienced research personnel to utilize their talents on problems of an applied nature; to facilitate the mobility of research workers between one institution and another and, at the same time to test the market for undertaking applied research.

SALARY AND ALLOWANCES

Salary will be at the rate of \$15,500 p.a. An allowance will be paid to the host institution to defray costs associated with administration, graduate assistance, laboratory maintenance, travel, etc.

TRAVEL ALLOWANCE

For successful overseas residents prescribed return fares for the Fellow and dependent family will be provided, including luggage allowances.

APPLICATIONS

Applications should be made on the approved application form which, together with the Objectives and Conditions of Award and Guide for Referees, may be obtained from Chief Scientific Liaison Officer, Australian Scientific Liaison Office, 64-78, Kingsway, London WC2B 6BD, England, or Scientific Attaché, Office of the Counsellor (Scientific), Australian Embassy, 1601 Massachusetts Avenue, N.W., Washington, D.C. 20036, U.S.A.

Applications must be forwarded to the Secretary, Reserve Bank Fellowships Committee, Reserve Bank of Australia, Box 3947 G.P.O., Sydney, New South Wales, 2001 by 30 June, 1974. Further information may be obtained from this office.

Applicants should arrange for at least two referees to forward their confidential reports to the Fellowship Committee before the closing date.

(1858)

POST-DOCTORAL FELLOWSHIPS
DEPARTMENT OF PHYSICS,
UNIVERSITY OF WATERLOO
 Waterloo, Ontario, Canada

Applications are invited for Post-doctoral Research Fellowships in Physics. Fellowships carry a stipend of \$8,520 per annum (\$8,700 after March 31, 1974), which is subject to Canadian income tax. The awards are tenable for a period of one year, with a possible renewal for a second year.

Research areas include: Astronomy and Astrophysics, Atomic and Molecular Physics, Biophysics, Crystallography, Electron Microscopy (thin crystal defects and interfacial structures), Ellipsometry, Condensed Inert Gas Properties, Laser Physics, Microwave Physics, Nuclear Magnetic Resonance, Solid State Physics (insulators, metals, non-linear dielectrics, and semiconductors), Statistical Mechanics, Superfluidity, Superconductivity, and Ultrasonics.

Closing date for applications is February 15, 1974.

For further information write to:

Dr. J. W. Leech,
 Chairman,
 Department of Physics,
 University of Waterloo,
 Waterloo, Ontario, Canada N2L 3G1. (1906)

UNIVERSITY OF OXFORD
 IN ASSOCIATION WITH NEW COLLEGE,
 ST. HILDA'S, ST. PETER'S, WADHAM,
 AND WORCESTER COLLEGES
IBM RESEARCH FELLOWSHIPS

Applications are invited for four IBM Research Fellowships tenable in any science department of the University for two years from October 1, 1974, in conjunction with Junior Research Fellowships at four of the following colleges: New College, St. Peter's, Wadham and Worcester Colleges (for a man); St. Hilda's College (for a woman).

The IBM Research Fellowships are open to applicants who will have a doctorate (or will have submitted a doctoral thesis) by October 1, 1974, but who will not have had more than three years' post-doctoral research experience by that date. At least one Fellowship will be offered in the biological sciences and at least one in the physical sciences. Scale of stipends: £1,968 to £2,544.

Application forms and further details are obtainable from the Secretary of Faculties (Ref. No. IBM/4), University Registry, Broad Street, Oxford OX1 3BD. Closing date for receipt of applications: January 14, 1974. (1863)

LA TROBE UNIVERSITY
 MELBOURNE, AUSTRALIA
LECTURER/RESEARCH FELLOW
(POSSIBLY TWO POSITIONS)
GENETICS AND HUMAN VARIATION

Applicants will be qualified in any field of the discipline, but a person with interest in human or animal genetics may be given preference for one position. A Research Fellow can expect a two-year appointment. In exceptional circumstances the appointment may be made at Senior Lecturer level. Information may be obtained from Professor P. A. Parsons, Chairman of the Department in the University. Salaries: Senior Lecturer, \$A12,268 by \$A408 (5) to \$A14,308; Lecturer, \$A8,698 by \$A470 (1) by \$A469 (6) to \$A11,982; Research Fellow, \$A8,128 by \$A285 (6) to \$A9,838 (tentative).

Further information and application forms are available from the Association of Commonwealth Universities (Appis), 36 Gordon Square, London WC1H 0PF, or from the Registrar, La Trobe University, Bundoora, Victoria, Australia 3083.

Applications close on January 31, 1974. (1799)

UNIVERSITY OF BATH
SCHOOL OF PHARMACY AND
PHARMACOLOGY
RESEARCH STUDENTSHIP

Applications are invited from good honours students in pharmacy, pharmacology or biochemistry for this industrially-sponsored award. The successful candidate will carry out a project concerned with the use of tryptophan in depression. The award is for one year at the normal S.R.C. rate and the appointee will be expected to register for an M.Sc. degree.

Applications should be made in writing to:

The Registrar (S),
 University of Bath,
 Claverton Down,
 Bath BA2 7AY,

quoting Reference 73/163. (1855)

NEW HALL, CAMBRIDGE

Applications are invited from women graduates for a RESEARCH FELLOWSHIP tenable at New Hall for three years from October 1, 1974. The maximum value of a Fellowship is £835 per annum with free residence, pensionable under the FSSU.

Particulars can be obtained from the President, New Hall, Cambridge, CB3 0DF, to whom applications should be sent by January 22, 1974. (1801)

UNIVERSITY OF BIRMINGHAM
DEPARTMENT OF BIOCHEMISTRY
POSTDOCTORAL FELLOWSHIP

Applications are invited for a Postdoctoral Research Fellowship to work on biochemical studies concerned with cell motility and the contractile proteins of non-muscle cells. A research background in cell fractionation procedures and protein isolation and characterisation is desirable. The appointment is supported by the Cancer Research Campaign for three years and the salary will be in the range £1,929 to £2,223 plus F.S.S.U. A starting date around January/February 1974 is envisaged.

Applications with the names of two referees should be submitted by December 12 to Dr N. Crawford, Department of Biochemistry, University of Birmingham, P.O. Box 363, Birmingham B15 2TT (Tel.: 021-472 1301 extension 3113) to whom further enquiries should be directed. (1831)

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF CHEMISTRY
POSTDOCTORAL FELLOWSHIP

Applications are invited for a Postdoctoral Fellow to work in one of the following fields: application of tunable lasers to high resolution spectroscopy; studies of the shapes of molecules and fragments in flames, plasmas and at high temperatures (this will include matrix isolation studies); studies of the shapes of molecules in liquid crystals and of ions in solution, using n.m.r. techniques; studies of transient species using pulsed laser techniques; studies of (organo-metallic) fluxional molecules. Salary on the scale £1,929 to £2,553 according to age and experience.

Applications giving a curriculum vitae and the names of two referees to the Departmental Administrator, Department of Chemistry, The University, Southampton, SO9 5NH. (1837)

UNIVERSITY OF SHEFFIELD
DEPARTMENT OF CHEMISTRY

Applications are invited for a POSTDOCTORAL FELLOWSHIP in the Department of Chemistry to join a group working on cell membranes. Suitable experience would be in biophysical chemistry and previous experience of studying cell membranes would be advantageous. The position is for a period of three years and is sponsored by the Wellcome Trust at a starting salary up to £2,508 per annum.

Applications, with curriculum vitae, should be sent to Professor D. Chapman, Department of Chemistry, University of Sheffield, Sheffield S3 7HF. Please quote R1/G. (1847)

UNIVERSITY OF SOUTHAMPTON
DEPARTMENT OF MATHEMATICS
SEMICONDUCTOR THEORY

Applications are invited for a POSTDOCTORAL FELLOWSHIP for theoretical work to investigate recombination in semiconductors and related problems by use of quantum mechanics and statistical mechanics. There will be contact with experimental work at various centres. The post is tenable for up to two years with possible renewal for a third year, commencing as soon as possible. The initial salary is according to experience but not in excess of £2,223 per annum plus F.S.S.U. for a recently qualified holder of a Ph.D. degree.

A RESEARCH ASSISTANT in the same area of work for someone familiar with computing procedures is also available at a salary up to about £1,000 per annum.

Applications by January 1, 1974, giving the names of two referees, should be sent to Professor P. T. Landsberg, Department of Mathematics, The University, Southampton SO9 5NH. (1836)

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School of Pharmacy

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Applications are invited from candidates with a good honours degree or equivalent in Pharmacy or Chemistry, to work for a higher degree on the project "4-phenylpiperidine derivatives as potential non-addicting, analgesics".

The project is a CASE award and the co-operating body is Allen and Hanburys Ltd. The stipend is £675 p.a. max. plus fees.

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LIVERPOOL, L3 9RH. (1853)

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Enquiries and applications to Professor N. Madsen, Department of Biochemistry. (1888)

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Further information and application forms for visits between July 1974 and February 1975 may be obtained from the Director, Science Department, The British Council, Lonsdale Chambers, 27 Chancery Lane, London WC2A 1PJ. The closing date for applications will be February 28, 1974. (1905)

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Medical Chemistry

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Microbiology
Molecular Biology
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Neuropharmacology
Organic Chemistry
Physical Biochemistry
Physical Organic Chemistry
Physical and Theoretical
Chemistry

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Population Biology
Taxonomy
X-ray Crystallography
Zoology

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Colloid Science
Computer Science
Electron and Ion Physics
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APPLICATIONS: Application forms and further particulars are available from the Acting Academic Registrar, Australian National University, P.O. Box 4, Canberra A.C.T. 2600, Australia, or from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF.

There is no set closing date. Applicants from outside Australia are advised to apply at least six months before they would expect to be able to take up a Scholarship if offered.

Completed applications from overseas should be sent direct to the University and not to the nearest Australian Embassy, High Commission or Consulate. Successful applicants will be notified of any requirements which they will have to satisfy for entry into Australia as private students. (1869)

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For further information please apply in writing to: **The Secretary, Institute of Connected Education, 28a Cadogan Place, London SW1X 9RX.**

(1911)

GRANTS & SCHOLARSHIPS

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Research grants are available for British students, at postgraduate, post-Grad.R.I.C. level for research in the following areas.

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- (10) Metal Carbonyls.
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Applications should be sent as soon as possible after the appearance of this advertisement to: Professor R. N. Haszeldine, F.R.S., Department of Chemistry, U.M.I.S.T., Manchester, M60 1QD. (1890)

LECTURES AND COURSES

EMBO WORKSHOP ON
"CELL ADHESION"

SCOTLAND: APRIL 17-19, 1974

A small workshop on this subject, sponsored by EMBO, to be held at Kildrummy, Aberdeenshire, has been arranged by Dr. G. Gerisch and Professor A. Curtis. A few places at the workshop will be available to workers who have recently entered the field and who are prepared to contribute to the meeting. Some assistance with finance may be available.

Application forms can be obtained from Professor A. S. G. Curtis, Department of Cell Biology, University of Glasgow, Glasgow G11 8QQ, Scotland, U.K. (1872)

London Mathematical Society

Professor René Thom

THE THEORY OF CATASTROPHES
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December 13, 5 p.m.

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(1970)

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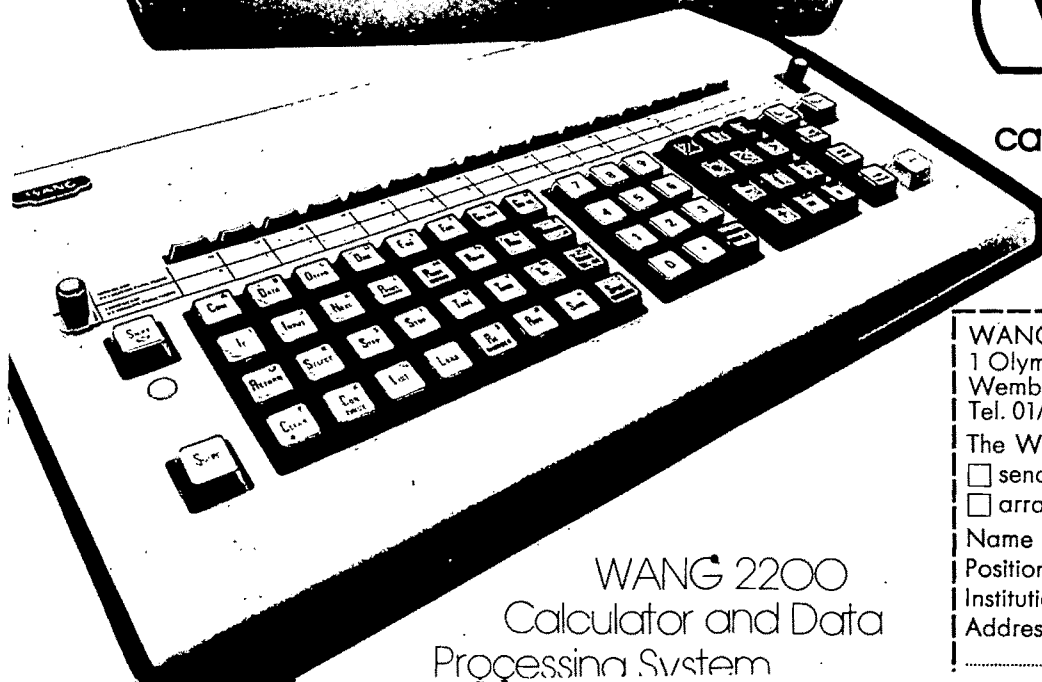
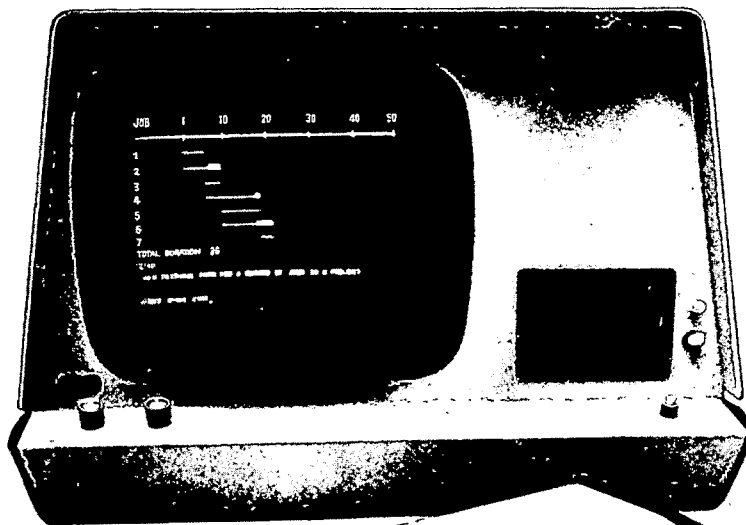
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GENETICAL STRUCTURE OF POPULATIONS

K. MATHER, F.R.S., Honorary Professor of Genetics, University of Birmingham.

Hardback: December 1973, 206 pages, 25 line illus, 412 12140 9, £4.00

Professor Mather has played a major part in extending and developing the idea of the genetic system, particularly in relation to the breeding system. He has pioneered the analysis of polygenic systems and their properties, and has related genetic structure to the different kinds of selection that impinge on a population. In this book he sets out not only to look at types of variation and types of selection but to examine the structure and changes of populations in relation particularly to the polygenic control of variation and to the genetic systems that govern its behaviour.

PHYTOCHEMICAL METHODS

J. B. HARBORNE, Reader, Department of Botany, University of Reading

Hardback: December 1973, 288 pages, 56 line illus, 412 10540 3, £4.80

The purpose of this book is to provide an outline and summary of methods available today for analysing plants for their organic constituents. Particular procedures used routinely in many phytochemical laboratories are recommended and sufficient details are provided for students to use the techniques for themselves. The book includes a selection of simple practical experiments and a bibliographic guide to more specialized texts.

GENETICS FOR MEDICAL STUDENTS

Seventh Edition

E. B. FORD, F.R.S., Professor in the Department of Zoology, University of Oxford

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This book has long established itself as a most useful general survey of genetics for medical students with no previous knowledge of the subject. In this seventh edition the work has been extensively revised throughout, with special attention being given to a more comprehensive introduction to serology in describing the blood groups, reflecting the current interest in this important field.

AN INTRODUCTION TO CORROSION AND PROTECTION OF METALS

G. WRANGLÉN, Professor, Department of Electrochemistry and Corrosion Science, Royal Institute of Technology, Stockholm

Hardback: 294 pages, numerous h/t and line illus, 412 12250 2, £3.00

This book is a systematic, balanced review of the whole area of metallic corrosion and its prevention. Various corrosion phenomena are explained in a simple and accurate manner and a comprehensive coverage of preventative measures is given. Although written as a short course for engineering students based on the author's lectures on corrosion science and technology, practising engineers concerned with metallic construction materials will also find the book of value.

ELECTROCHEMISTRY

J. KORYTA, J. DVORAK AND V. BOHACKOVA

Science Paperback: November 1973, hardback 1970, 360 pages, 89 line illus, 412 21130 0, £3.00

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THIN FILM PHYSICS

O. S. HEAVENS, Professor of Physics, University of York

Science Paperback: November 1973, hardback 1970, 160 pages, 8 h/t illus, 412 21110 6, £1.50

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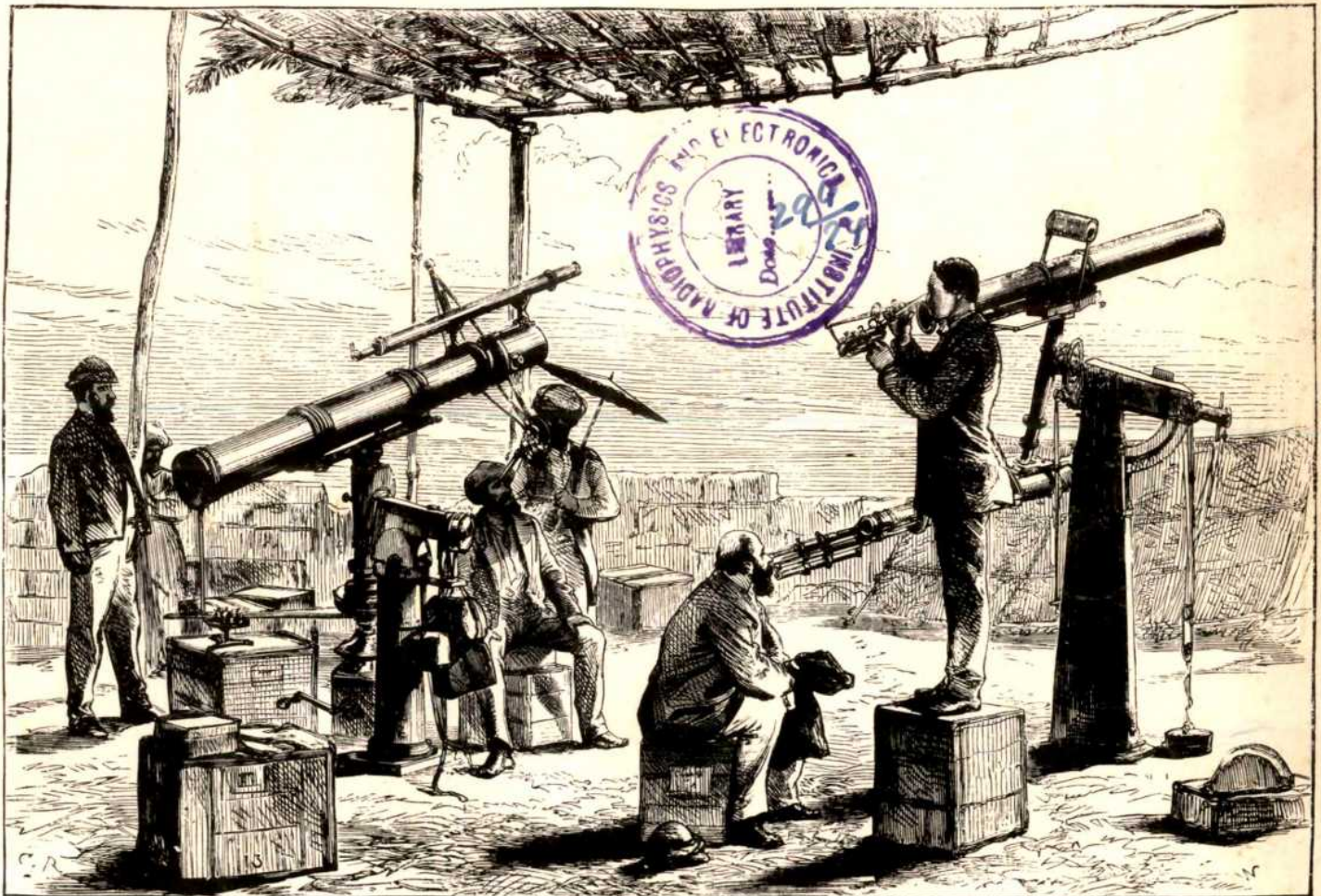
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NATURE

Vol 246 No 5433

December 14 1973

FRIDAY



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Christmas miscellany

Molecular evolution and fossil record

Origin of comets

Microorganisms in hailstones

Cell

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Cell is published at monthly intervals by The MIT Press. The contents of the first issue, of January 1, 1974 are:

Genetically directed preferential X-activation seen in mice: U. Drews, S. R. Blecher, D. A. Owen and S. Ohno

Ouabain-resistant mutants of mouse and hamster cells in culture: R. M. Baker, D. M. Brunette, R. Mankovitz, L. H. Thompson, G. F. Whitmore, L. Siminovitch, and J. E. Till

A uridine kinase-deficient mutant of 3T3 and a selective method for cells containing the enzyme: L. Medrano and H. Green

SpoT, a new genetic locus involved in the stringent response in *E. coli*: T. Laffler and J. Gallant

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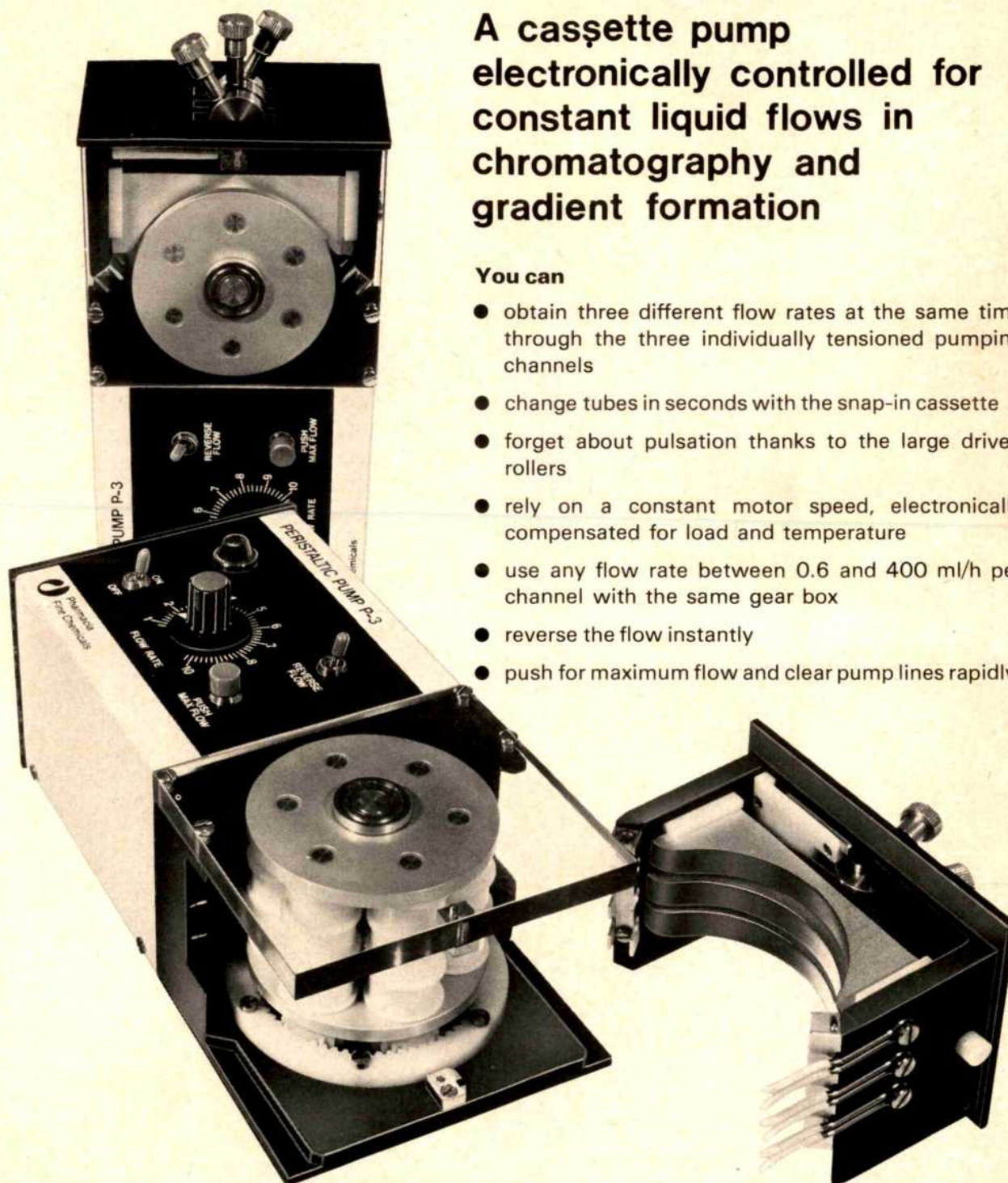
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The first issue of each of the translation journals will be published in early 1974, and, as with our Russian periodicals under the Consultants Bureau imprint, the translations of the Chinese journals will be available within six months following the appearance of the original Chinese edition.

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available in 1974

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NATURE

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FRIDAY DECEMBER 14 1973

Vol. 246

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	Page
Can Physics be Fun?	369
Making Plans for Energy Research	370

NEWS

Radical Rethinking Needed in University Science/Nuclear Power/Engineering/Short Notes/British Council/Deafness	372
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Climatic Change in China over the Past 5,000 Years/Records of the 1973 Eclipse/Particle Creation in a Big-Bang Universe / Demography / Geopolitics / Astronomy / Insect Eye / Population Ecology / Purple Membrane / Food Biochemistry / Insecticides / Animal Physiology / Viruses / Drug Resistance / Meteorology	375
---	-----

MISCELLANY

Christmas Prize Quiz	385
What's in a Name?	385
Solution to the BA Cartoon	386
Chess Problems	388

ARTICLES

Molecular Evolution of Myoglobin and the Fossil Record: a Phylogenetic Synthesis—ROMERO-HERRERA, LEHMANN (MRC Abnormal Haemoglobin Unit, Addenbrooke's Hospital, Cambridge), JOYSEY and FRIDAY (University Museum of Zoology, Cambridge)	389
Is the Universe a Vacuum Fluctuation?—TRYON (City University of New York)	396

	Page
Peace Research and SIPRI—BARNABY (SIPRI, Stockholm)	397
Comet Kohoutek—BIERMANN (Max Planck Institute, Munich)	400
Deep sea sediments—Variations in Be and Al isotopes may result from cosmic rays caused by supernova—HIGDON and LINGENFELTER (California, Los Angeles)	403
Cyclic nucleotides—Intracellular mediators of expression of antigen-sensitive cells—WATSON, EPSTEIN and COHN (Salk Institute)	405

LETTERS TO NATURE

Physical Sciences

Comets—Nature and origin—ALFVÉN and MENDIS (California, San Diego)	410
Solar eclipse—Visual determination of the mean effective chromospheric thickness—BECKMAN (Queen Mary College, London).	411
—Search for atmospheric gravity waves—BECKMAN and CLUCAS (Queen Mary College, London)	412
—Rapid variations observed during the eclipse of June 30, 1973—KOUTCHMY, FAGOT (CNRS, Paris), DZUBENKO, NESMJANOVICH, RUBO and VSEKHSVJATSKY (Kiev)	414
Intergalactic medium—Possibilities of study using flares on remote objects—GINZBURG (P. N. Lebedev Institute, Moscow)	415

The illustration on the cover of this issue was first published in *Nature* on February 1, 1872 (5, 266; 1872).

(Continued overleaf)



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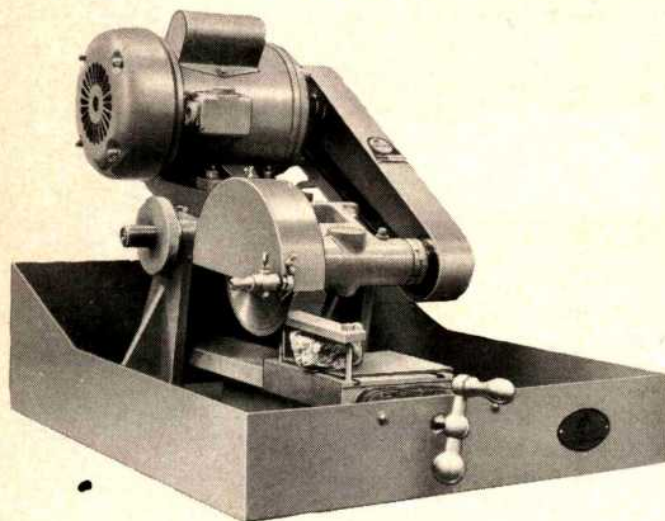
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	Page
Biological Sciences	
Hailstones —Distribution of microorganisms—MANDRIOLI, PUPPI, BAGNI (Bologna) and PRODI (CNR, Verona)	416
Procollagenase —Phagocytic release and activation of human leukocyte procollagenase — ORONSKY, PERPER and SCHRODER (Ciba-Geigy, New York)	417
Heavy chain disease —Detection in normal plasma of immunoglobulin resembling the protein of γ -chain disease—LAM and STEVENSON (Southampton General Hospital)	419
Fertility —Isolation of fractions rich in human Y sperm—ERICSSON, LANGEVIN and NISHINO (Schering A.G., Berlin)	422
Digestion —Gastrin activity in chicken proventriculus—OLOWO-OKORUN and AMURE (Ibadan)	424
Addiction —Morpine-induced suppression of voluntary alcohol drinking in rats—SINCLAIR (ALKO Laboratories, Helsinki), ADKINS (Sangamon) and WALKER (Oregon)	425
Jumping millipede — <i>Diopsiulus</i> Silvestri jumps by a modification of the normal millipede defence reaction of spiralling—EVANS and BLOWER (Manchester)	427
Bone gnawing —Gnawing of bones and antlers by deer—SUTCLIFFE (British Museum (Natural History))	428

BOOK REVIEWS

	Page
Einstein: The Life and Times, Ronald W. Clark (A. J. MEADOWS)	431
Topics in Geophysics, P. J. Smith (E. C. BULLARD)	432
Out of the Zenith: Jodrell Bank, 1957–1970, Bernard Lovell (M. ROWAN-ROBINSON)	432
Science and Philosophy in the Soviet Union, Loren Graham (JOHN ZIMAN)	433
Illusion in Nature and Art, R. L. Gregory and E. H. Gombrich (editors) (N. W. PIRIE)	434
Water: Comprehensive Treatise, vols 2 and 3, Felix Franks (editor) (H. J. V. TYRELL)	435
Aldous Huxley: a Biography. Volume 1 1894–1939, Sybille Bedford (WILLIAM COOPER)	435
The Life Game, Nigel Calder (GILLIAN MOORE)	436

CORRESPONDENCE

ERTS (R. W. Nicholls, P. A. Mohr)/Whiter than White (W. Hill)/Paperback Polymorphism (A. W. F. Edwards)	437
Announcements —University News / Appointments / Miscellaneous	438

Next Monday's issue will include

- Oceanography**—Pole tide—MILLER and WUNSCH (MIT)
- Geochemistry**—Two distinct mantle sources under Iceland and the Reykjanes Ridge—HART (Carnegie Institution, Washington), SCHILLING (Rhode Island) and POWELL (Oberlin College)
- White dwarfs**—White dwarfs as X-ray sources—DEGRE-GORIA and WOLTJER (Columbia)
- Geophysics**—Is the Betancuria Massif, Canary Islands, an uplifted piece of oceanic crust?—GASTESI (Oxford)

Next Wednesday's issue will include

- Synaptic response**—Modulation by fast transient K^+ current in snail neurones—DAUT (Max Planck Institute, Munich)
- DNA sequencing**—Isolation and transcription of 3' terminal regions of unique DNA molecules—CASSUTO, ROSENBERG and YOT (Yale)
- Genetics**—Suggested mechanism for increase in size of genome—MACLEAN (Southampton)
- Neurophysiology**—Influence of strychnine on dorsal root potentials and amino acid responses in frog spinal cord—NICOLL and BARKER (St Elizabeth's Hospital, Washington DC)

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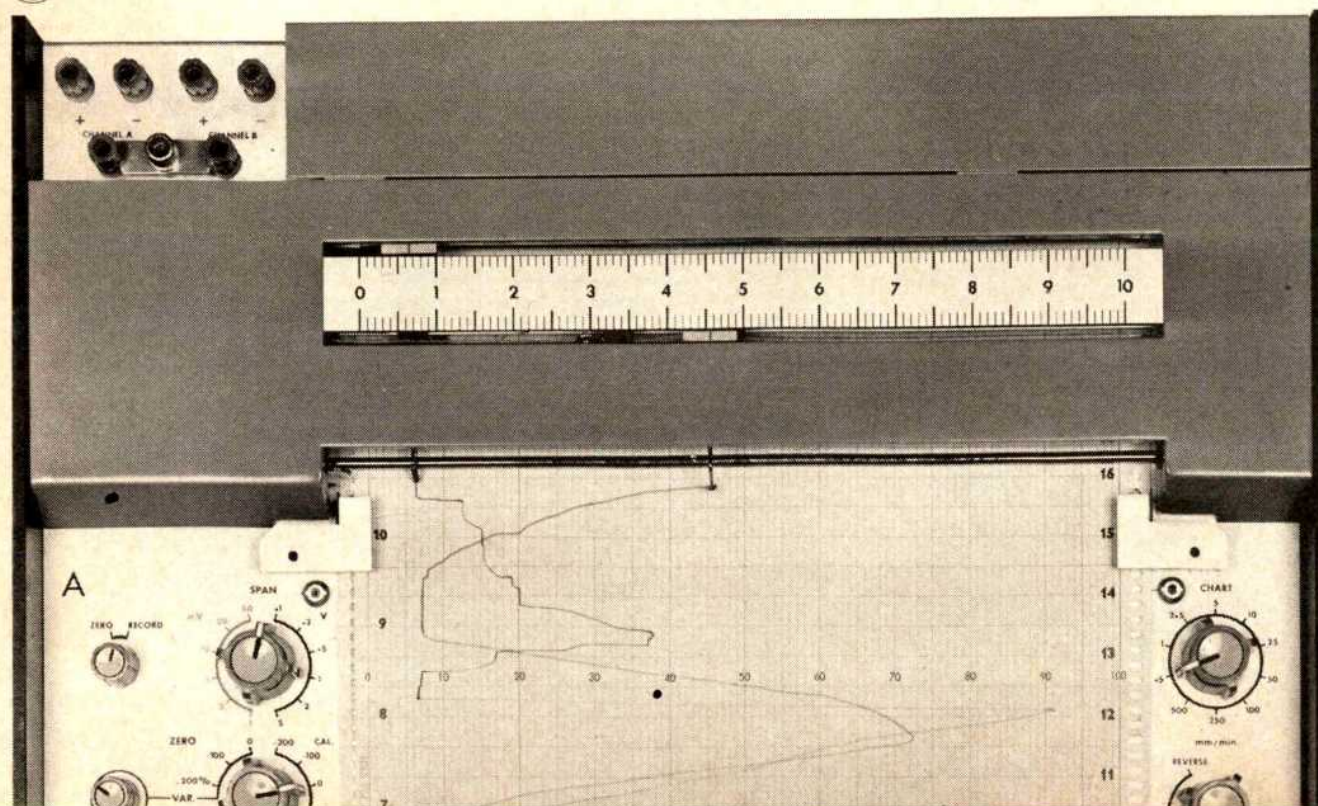
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PHILIPS



Can Physics be Fun?

THE Institute of Physics has recently produced a handsome book on humour and humanity in physics, which offers a rare opportunity to look at a large collection of pieces by physicists writing with a wider audience in mind (*A Random Walk in Science*, an anthology compiled by R. L. Weber and edited by E. Mendoza, pp. 206 (Institute of Physics, Bristol) £4.75). The contents are distinctly variable—at the one end some fascinating insight into the prosecution of science, at the other ghastly laboured in-jokes. Pieces such as Jeremiah Horrocks's description of his observation (sandwiched between preaching sermons at Mattins and Evensong) of the transit of Venus in 1639 and R. W. Wood's account of his encounter with Blondlot, of N-ray notoriety, are real delights and there are many others too. Donald Glaser's problems with getting the bubble chamber accepted and William Whewell's strictures against teaching modern discoveries to students are reminders that science never develops smoothly. For these the book can be recommended, but when physicists try to be funny, how banal they can be and how contrived their nonsense papers, bogus definitions and doggerel seem on paper.

Yet physics—in fact all the sciences—can produce no end of fun in the laboratory. The problem seems to be conveying this fun to others without diluting the impact.

Can humour be categorised? It is customary to speak of the juxtaposition of the ridiculous with the normal as the basis of humour—the virus that we illustrate on page 382 is a good example of this. Sometimes, however, the juxtaposition of the normal with the normal is just as funny, and there is potentially as big a laugh in the predictable happening as the unpredictable. This is perhaps particularly true when the predictable comes from, for instance, a group of people each of whom has individually the capability to behave unpredictably.

Words play a large part in all humour, of course, but apart from the very few really talented people who can use words for conscious humour—and they will not be looking for a career in science when the rewards are so great elsewhere—one can get great pleasure from the unconscious humour of words. Dr Spooner's accusation "you've hissed all my mystery lectures" is pure gold. Even the despicable Post Code, the ugly accretion that the British Post Office is trying, rather unsuccessfully, to foist on the public, has its lighter moments. The Natural Environment Research Council has the Post Code WC1H0AX.

Scientists are peculiarly prone to two extraordinarily persistent strains of humour—the pun and the limerick. It is difficult to find any extenuating circumstances for the pun despite its regular outings in the headlines of *The Guardian*. One would have thought that the towering achievement of the bilingual pun in the book *Mots d'Heures, Gousses, Râmes* would have silenced lesser perpetrators.

The limerick is an altogether healthier animal and it is not too difficult to see why it has such an appeal. It

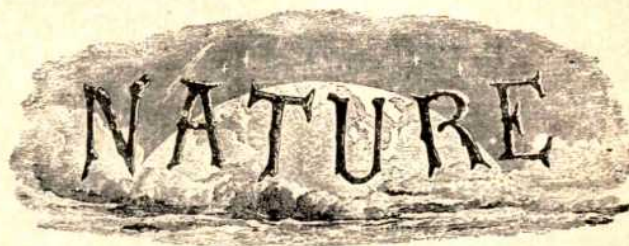
is palpably not poetry and so there is none of the embarrassment that would be attached to the combining of vulgarity with the immortal art form of, say, the sonnet. And yet it has the neatness of expression and the brevity of utterance of poetry. Relativity, with all its manifest absurdities to the man in the street, has been fertile territory for the limerick. Although the journey of the lady called Bright is well known to all physicists, it is sad to see the general decline and absence here of the marginally more plausible:

There once was a fellow called Fisk,
At fencing exceedingly brisk.
So fast was his action
The Fitzgerald contraction
Reduced his épée to a disk.

It would be impossible to write on humour in physics without giving a very honourable mention to Professor R. V. Jones, who rightly gets several pages to himself in the institute's book. He more than anyone else seems to be capable of capturing the laboratory joke and telling it amusingly. The Aberdeen chimney affair is every bit as funny as Gerard Hoffnung on the bricklayer's excuse. His Cambridge examination question does not make it into the book and deserves a wider circulation:

"It says in *Proverbs*, 30 vv 18–19,
'There be three things which are too wonderful for me
Yea, four which I know not;
The way of an eagle in the air;
The way of a serpent upon a rock;
The way of a ship in the midst of the sea;
And the way of a man with a maid,'
Discuss any three."

100 Years Ago



THE adult female Indian Rhinoceros, which has been in the Zoological Society's Gardens since July 1850, then not larger than a full-sized dog, died on Sunday last, having been ill for some time previously. The coldness of the weather and the fog were probably the exciting causes of its death, though no definite pathological changes have been found on *post-mortem* examination. There were no symptoms of senile decay.

From *Nature*, 9, 132, December 18, 1873.

Making Plans for Energy Research

Colin Norman, *Nature's* Washington Correspondent, looks at the research programmes which may soon be adopted in the drive to make the United States self-sufficient in energy.

SCIENTISTS and engineers working on energy problems in the United States have good cause to be thankful for the energy crisis in general and the Arab oil boycott in particular, for they are about to stimulate massive increases in federal funds for energy research and development. At the beginning of last week, Dr Dixie Lee Ray, Chairman of the Atomic Energy Commission (AEC), delivered to the White House a five-year plan for energy research and development which had been personally requested by President Nixon. It would almost double present expenditures, soaking up at least \$10,000 million of federal funds before 1980. And, at the end of the week, the Senate unanimously passed a bill which sets aside \$20,000 million for non-nuclear energy development over the next 10 years.

Although the AEC's plan and the Senate bill set slightly different courses, their goal is the same: to make the United States independent of foreign suppliers of fossil fuels as soon as possible. In one of his latest energy messages, President Nixon called the effort Project Independence, and he indicated that the goal of self-sufficiency could be attained by the end of the 1970s. The AEC's report, however, says that 1985 "is the earliest date by which self-sufficiency can reasonably be expected", and Senator Henry Jackson, author of the Senate bill, doubts that the AEC plan will be able to buy independence at all.

One problem is that simply pouring money into research and development is not enough on its own to ensure self-sufficiency. To exploit the new technology that flows from the research will require massive capital investment by industry and complex decisions by the federal government. It will also raise difficult legal and environmental problems, and cause political difficulties by putting the federal government even more firmly hand in glove with the energy industry.

The AEC's plan, nevertheless, represents a significant break with tradition, not least because it opens up the Administration's budgetary deliberations to public scrutiny. The plan was requested by President Nixon in June, when he was publicly calling the energy

shortages a "challenge" rather than a crisis. He directed Dr Ray to produce a national energy strategy, a five-year plan for research and development, and a set of recommendations for inclusion in the Administration's 1975 budget—all by December 1. Ray complied, after a complex and frenzied series of planning sessions attended by people from government, industry and academe, and the plan is now at the Office of Management and Budget where it is being studied in detail as part of the preparations for the 1975 budget.

It is a remarkably candid, lucid and optimistic document which proposes huge concentration on short-term objectives to increase fuel supplies and to cut down on inefficient energy use. It is quick to point out where some of the blame for the energy crisis lies: "The energy shortages of today and those projected for future decades stem, in part, from the lack of a coordinated national programme for energy research and development over the past 10 or 20 years". And it adds that the shortages "impart a long overdue sense of

urgency to the effort being launched to meet not only immediate requirements but also the growing needs of the years ahead".

The strategy is to concentrate nearly half of the proposed \$10,000 million on short term goals, such as reducing consumption, substituting coal for oil and increasing production of oil and gas. Almost 40% of the funds are earmarked for medium term efforts such as coal gasification and oil shale development. And a small fraction—7%—would be spent on longer term options such as fusion power. In addition, the plan indicates that private industry can be expected to put up as much as \$12,500 million for energy research and development over the next five years, thanks to the incentives provided by rapidly increasing energy prices. That would bring total expenditure on energy research and development in the United States to more than \$22,500 million before 1980.

Five tasks are outlined in the plan, as follows (see Table 1):

- Conserve energy and energy resources—this would gain \$1,440 million, in comparison with some \$95 million under previous spending plans.
- Increase domestic production of oil and gas. \$460 million would be spent in this area by the federal government, a five-fold increase.
- Substitute coal for oil and gas on a

Table 1 Federal Energy Research and Development Obligations by Individual Programme Element, Fiscal Years 1973-1979 (in \$ millions)

Self-sufficiency task	Actual 1973	Planned 1974	Recommended 1975	Recommended 1975-79 programme	Previous 1975-79 plans for comparison
1. Conserve energy and energy resources	52.8	62.3	166.2	1,440	9.50
Reduced consumption	12.1	22.3	29.9	210	15.0
Increased efficiency	40.7	40.0	136.3	1,230	80.0
2. Increase domestic production of oil and gas	20.0	19.5	51.7	460	90.0
Production	12.8	11.2	31.7	310	50.0
Resource assessment	7.2	8.3	20.0	150	40.0
3. Substitute coal for oil and gas on a massive scale	88.8	167.2	405	2,175	842.0
Mining			45	325	
Direct combustion			30	200	
Synthetic fuels			240	1,270	
Common technology			90	380	
4. Validate the nuclear option	395.8	517.3	731.7	4,090	3,672.3
Safety, enrichment, high temperature gas reactor	129.7	151.7	216.2	1,245.7	1,201.7
Breeder	266.1	365.6	515.5	2,844.3	2,470.6
5. Exploit renewable energy sources to the maximum extent feasible	82.8	123	217.5	1,835	1,232.0
Fusion	74.8	98.7	145.0	1,450	1,132.0
Solar	4.2	13.2	32.5	200	80.0
Geothermal	3.8	11.1	40.0	185	20.0
Total	640.2	889.3	1,572.1	10,000	5,931.3
Supporting programmes (incremental federal funding to present programmes)					
Environmental effect			105.9	650	
Basic research			43.0	300	
Manpower development			5.0	50	
			153.9	1,000	

Table 2 Estimated Contribution to Energy Inputs (Million Barrels per Day Oil Equivalent)

Energy source	1972 Actual Inputs	1980			1985		
		Total with former Pro- gramme	Increment from recom- mended Pro- gramme	Total with recom- mended Pro- gramme	Total with former Pro- gramme	Increment from recom- mended Pro- gramme	Total with recom- mended Pro- gramme
Total energy	34.1	47.0		47.0	57.0		57.0
1. Conservation			4.7	(4.7)		7.0	(7.0)
Production requirements	<u>34.1</u>	<u>47.0</u>		<u>42.3</u>	<u>57.0</u>		<u>50.0</u>
2. Domestic production of oil and gas	21.4	21.5	0.5	22.0	21.5	5.1	26.6
3. Domestic coal production and conversion	5.9	9.1	0.5	9.6	11.4	2.5	13.9
4. Nuclear	0.3	3.6	0.2	3.8	7.1	0.6	7.7
5. Renewable resources (solar, geothermal, hydro-electric)	1.4	0.8	0.2	1.0	1.0	0.8	1.8
Imports	5.1	12.0	(6.1)	5.9	16.0	(16.0)	0.0

massive scale. Coal is the most abundant energy resource in the United States and the objective would be to reverse the trend of the past few years which has seen power plants and factories switching from coal to cleaner fuels. Some \$2,175 million is recommended to develop technologies to stimulate production and use of coal, up from \$842 million.

● Validate the nuclear option. Although the plan suggests that \$4,000 million should be spent on nuclear technology over the next five years, the actual increase is not large. "This reflects the generous level of funding for the nuclear programme over past years, compared to other programmes", the head of the AEC said in her report.

● Exploit renewable energy resources to the maximum extent feasible. The report recommends that fusion research and the development of geothermal energy and solar power should receive \$1,835 million, compared with \$1,232 million under previous plans.

The basic strategy is to press ahead simultaneously with all technologies that look promising and to "pursue most individual research efforts in an accelerated but orderly manner, avoiding the risks of 'great leaps forward' that do not materialise". Nevertheless, high risks should be taken with technologies that are likely to have a very high potential value, such as *in situ* oil shale retorting (see *Nature*, 246, 323; 1973) and techniques for extracting natural gas from tight deposits. Ray also suggests that sufficient parallel studies should be conducted so that, even if some fail, the overall goal will not be jeopardised.

A novel part of the plan is to initiate a "Synthetic Fuels Pioneer Programme" in an effort to help bridge the gap between research on coal gasification and liquefaction, and application of the technology. The idea would be to provide industry with federal guarantees of prices or loans to begin constructing demonstration plants next year. The plants would be built, operated and owned by private concerns and consortia but part of the deal would allow the government to use them for experi-

mentation. With luck, the technology would be developed by 1976 and the groundwork would be laid for a massive private investment programme.

The overall plan represents a huge undertaking, by any criterion, but will it achieve the goal of self-sufficiency? The first thing to be said is that in spite of President Nixon's sanguine public statements, the impact on fuel supplies by 1980 will be relatively small, and the major contribution to offsetting energy imports will come from conservation measures. Nevertheless, Ray predicts that a combination of conservation and increased domestic energy supply could achieve the nirvana of self-sufficiency by 1985 (see Table 2).

The equivalent of 16 million barrels of oil a day will have to be either conserved or added to the domestic energy supply to reach the goal in 1985. The plan indicates that 7 million of them will come from conservation measures and 9 million will be added to supplies if the technology is developed and exploited. If the predictions are borne out by experience in the next ten years, it will be an impressive monument to American ingenuity.

Not everybody is quite so optimistic, however, and looming large among the doubters is Senator Henry M. Jackson, the Democratic Senator from Washington who has carved out a niche as the most powerful member of the Senate in energy matters. He believes that the \$10,000 million ceiling imposed on the programme by the White House is too miserly and his bill, which was passed by the Senate last week, would increase expenditures even more. Although the AEC's plan envisages spending \$10,000 million over five years and Jackson's bill calls for \$20,000 million over 10 years, the essential difference is that the former covers nuclear energy whereas the latter covers only non-nuclear technology.

Jackson's bill would, in short, set up a federal Energy Research Management Project, headed by an independent chairman, and give it the power to direct and coordinate all the government's energy research and development programmes. It would have control over

some \$800 million a year, over and above the present budgets given to individual agencies. An important feature of Jackson's bill is a provision that would authorise the establishment of joint government-industry development projects, so that federal funds could be provided directly for the construction of demonstration plants to exploit technology for coal liquefaction and gasification, oil shale development, and geothermal and solar power. Jackson believes that one of the chief weaknesses of the AEC plan is that it assumes that industry would be willing to spend vast amounts of money on the construction of development plants; direct government support will be required, he suggests.

The prospects for Jackson's bill as it moves through the rest of the Congressional mill are at present unclear—it must now be approved by the House of Representatives—but a similar measure is likely to be approved this week by the House Commerce Committee. There may, however, be a move in the House to put off consideration of the measure until an extensive government reorganisation plan, involving the merger of several departments and agencies into a Department of Energy and Natural Resources, has been dealt with. In any case, the bill only authorises expenditures and the actual money would have to be approved by appropriations committees and Congress itself.

What are the prospects for the AEC's proposals? They will begin to appear in the Administration's 1975 budget request which will be unveiled at the end of January. The plan calls for a total of \$1,572 million to be spent in 1975—nearly double this year's estimated expenditures—and, again, it will have to be approved by Congress.

One thing is certain, however—universities, industries and other institutions conducting research on energy are in for a veritable bonanza. Whether the thaw in energy funds will be accompanied by a sudden freeze in other research expenditures is, however, a matter of some concern. The answer will come in the budget in January.

NEWS

Radical Rethinking Needed in University Science

"UNLESS the quality of research (in British universities) puts it in the 'world league' the case for supporting it from public funds is weak." This is one of the statements made in a report published this week by the British Association for the Advancement of Science (*Higher Education and Scientific Research*, BAAS, Fortress House, Savile Row, London W1X 2AA, 30p).

The report, the first to be published by the British Association in a new series, is the result of the deliberations of a study group set up under the chairmanship of Lord Ashby to discuss the implications for scientific research of the white paper, *Education: A Framework for Expansion*, published in 1972.

The study group expresses concern that research was not given sufficient consideration in the white paper—the word research, it is pointed out, is only mentioned once in the document. The study group observes that this is in spite of the fact that by 1977 there will be 52,000 postgraduates in British universities, 20,000 of them being scientists and probably 15,000 of these engaged in research for higher degrees.

Universities should remain as centres of scientific research, says the study group, and "it would be a calamity for science in Britain, as well as for higher education, if the government's plans for expansion underestimated this need". Although supported research in Britain should be of international standard, according to the study group, this does not mean that universities should concentrate entirely on research to the detriment of other activities. Those university teachers who are not gifted research workers should not desist from the "pursuit of knowledge," says the report, "but rather . . . not all those who pursue knowledge should feel under an obligation to carry out research leading to original publications, or should expect their activities to be financed by grants from research councils or the like".

The viability of research departments with small numbers of graduate students is also called into question in the report. Research students benefit from contact with each other, and facilities for formal postgraduate teaching may be lacking in small departments. These are put forward as reasons why larger departments are to be preferred. Of the sixty or so university physics departments which receive Science Research Council studentships almost one-third receive five or fewer studentships (nuclear physics departments excepted).



Lord Ashby

"If (and we emphasise that this is an arguable matter) the critical mass of a graduate school in a physics department is at least ten postgraduates then it would follow that postgraduate students in many small departments are not getting as good an apprenticeship for research careers as are their fellows in large departments."

The study group points out that there is a case for concentration of resources in centres of research but that this must be balanced by "the need to sustain scholarly standards and enthusiasm among academics in departments which are not designated as centres of research".

For instance, says the study group, research councils might plant viable research units in small departments "even at the risk of depleting any additional resources available to the centres of research". More frequent sabbaticals—perhaps one term free every seven—and an encouragement for staff of small departments to 'migrate' to larger departments as guests could also be a way of resolving the issue.

The unmistakable conclusion which the study group comes to is that in the future there may need to be a significant number of teachers in universities who are not established "in the hierarchy of research workers but rather in the

hierarchy of interpreters of research to advanced students".

The research councils and the University Grants Committee should now give consideration to supporting graduate schools in some universities but not in others, says the study group. Research should be financed with this in mind and limited resources should not be diffused "as widely as . . . at present". But the initiative is not to be left entirely in the hands of the research councils and the UGC, and the universities are called upon to initiate some of these changes themselves.

Such radical changes, however, will need to be compensated for. The study group lists two such solutions as follows:

- Academics who are not at centres of research in their subjects must be compensated by providing, and financing, opportunities for them to keep close to the growing points of research and, if they so wish, to come as guest workers to centres of research.
- Implicit value judgments which at present overemphasise achievement in published research as a criterion for a career in university or polytechnic teaching must be modified.

But the essence of the report is that the issues raised need to be discussed. The differing rates of growth of the research and university budgets in the years ahead will ensure that the problems of keeping all university staff members actively involved in "world league" research will increase.

£25,000 Prize

THE MacRobert Award for 1973 has been won by three members of Dunlop Ltd for their development of the Denovo tyre and wheel system. They are Tom French, Eric Mitchell and Reginald Edwards, and they share £25,000—the largest prize of its kind in the world. It is awarded annually for an outstanding contribution in engineering or the physical sciences enhancing the prestige and prosperity of the United Kingdom.

The Denovo system permits tyres that have blown out or been punctured to be driven for up to 100 miles at up to 50 miles per hour without attention or permanent damage to the tyre, and is beginning to be offered as an option on cars in Britain.

NUCLEAR POWER

LWRs Are Coming

ONLY by building light water reactors (LWRs) bought from abroad can Britain be sure of a supply of nuclear generated electricity on time, Sir Arnold Weinstock told the Select Committee on Science and Technology this week. Sir Arnold, who is managing director of GEC, the company that holds half the shares in the National Nuclear Corporation, told the committee that since March when he last gave evidence to the committee he had come to the conclusion that the British designed advanced gas cooled reactor (AGR) "does not provide anything like the necessary security of supply". Five AGR stations are under construction. All of them are overdue.

Sir Arnold said that last March he had hoped that it would be possible to build a series of AGRs. But the difficulties with the stations had not been resolved. "This is rather worrying if you are contemplating a programme that will depend on good delivery dates."

Nine countries are building light water reactors and stations totalling 250,000 MW are on order. From 1974 it is expected that 50,000 MW a year of light water reactors will be ordered. There is much more experience of these reactors and there is obviously a worldwide market available, he said.

Sir Arnold confirmed that if the government does decide to allow the Central Electricity Generating Board to order light water reactors, the first station will come, at least in part, from the United States. The steel pressure vessel and the steam generator would be imported along with various other high quality components. About 20% of the cost of the first station might be spent on imports. For the second station the percentage would be lower, although it is possible that even for subsequent stations the pressure vessels will continue to be imported. But the pressure vessel only costs £2 million out of £150 million for the complete station.

Sir Arnold emphasised that the imported parts need not come from the United States for stations after the first one. France, Holland and Germany all have facilities to manufacture LWR parts.

Asked if importing United States reactors would not be a body blow to British advanced technology, Sir Arnold replied that further development work on nuclear systems — including the light water reactors — is still needed and Britain can contribute to this as part of an international programme. He also agreed that a commercial high temperature reactor of about 1,300 MW should be built.

On the question of safety Sir Arnold

said that the doubts raised in this area were the one inhibiting factor. But the Central Electricity Generating Board has made careful studies of the light water reactors and they are satisfied, he said. Sir Arnold added that as far as he could tell most of the safety questions had been dealt with or were being dealt with satisfactorily except the possibility of the pressure vessel fracturing. But most experts in Britain and the United States are satisfied that the vessel is safe, although doubts have been raised recently. "I would not for a second advocate that we should have a programme of nuclear machines or any other machines that would put the public at risk."

Buying light water reactors would not remove all possibility of building gas cooled stations, Sir Arnold said. If there were a serious accident with light water reactors anywhere in the world that necessitated ending a British light water programme we could always return to AGR stations or to Magnox. Magnox stations have been considered for this programme, but the cost and the need to redesign them extensively (which would again introduce the problems of building prototype plant) led to their fall from favour.

ENGINEERING

Unhappy Lot

ENGINEERS, it seems, are not very happy people. Underpaid, under-recognised, and belittled beside their European counterparts, the 300,000 strong profession in Britain is eager to have its wrongs righted.

That at least was the impression given last week when the Council of Engineering Institutions (CEI) published the results of a survey of 27,000 of its members.

Mr B. Hildrew, a former chairman of the Institute of Marine Engineers and the director of the survey, said that the income of engineers has only risen 1.5% in real terms since 1966. "Considering that we are a technological nation this must be a serious warning."

The CEI also collected, among the welter of statistics on numbers employed in each industry, salaries earned and fringe benefits received, an estimate of the satisfaction felt by engineers with their jobs and prospects.

On the whole, the survey shows, two out of three engineers are well satisfied with life, but in certain industries, notably machine tools and gas distribution, engineers are unhappy with the current situation. And in a number of industries—particularly machine tools, some mechanical engineering, the aircraft industry and vehicle manufacture—some engineers are disenchanted with their career prospects.

On the continent, the CEI maintains, engineers are paid better and have a higher status.

The survey also reveals that the percentage of engineers under the age of thirty has fallen, reflecting the relative lack of interest in the subject at undergraduate level in universities. But the under-thirty intake now includes a very high percentage of graduates, as the engineers are gradually turning themselves into an all-graduate profession. From 1974 all new entrants to institutional membership will hold graduate or equivalent qualifications. In 1966, graduates were outnumbered two to one by non-graduates among members of the institutions. Now the figure is one to one.

The number of engineers in research and development has declined as engineers are transferred into production and construction work to meet the demands created by economic expansion. Members of the CEI see this as a welcome and productive change.

Immaculate Hanker

Received recently in a British university:

Dear Sir,

With due respects and most supplicably I intend to bring the matter under your consideration that I have the honour of seeking admission in your institution to complete the MS(Physics) degree course there.

I am very much interested in pursuing higher studies from your esteemed university. It has been my lifelong ambition to do MS and advanced research in the field of science from a university of a technologically advanced country. I conceive an immaculate hanker to achieve a chance to complete this course in your highly esteemed institution and if in some way, I get admission there, it will be an affair to stimulate me to an inexplicable exhilaration.

I shall very much appreciate your help in securing for me some sort of financial assistantship in the form of a Fellowship, part-time job or as you may deem fit. In return I have nothing to offer except hard work, full cooperation and everlasting indebtedness towards you.

Perhaps this will be an adequate information I am required to give. I hope you will entertain my long cherished ambition in exorable way, and I am waiting an optimistic expectation for an adorned favourable reply from you.

Yours obediently

Unemployment among engineers has halved to 0.52% over the two years since the CEI's last survey, while the general distribution of engineers throughout industry has not changed much. The massive recession in machine tool manufacture in 1971 has halted, although there has been no appreciable recovery, and the percentage of engineers employed in electrical equipment manufacture and in electricity generation or distribution has dropped. Since 1971, consultancy has taken over from electronics as the largest single employer of engineers (about 10%).

The survey also reveals that engineers who earn more than £3,000 a year also on average receive the equivalent of a further 20% of their salaries in fringe benefits.

Short Notes

Alternative to Hexachlorophane

A NEW disinfectant-detergent preparation for use as a surgical scrub in place of hexachlorophane has passed its first reported independent field trial with flying colours. Hibiscrub, a chlorhexidine detergent solution, marketed by ICI, has been tested by an operating team in the professorial surgical unit at Aberdeen Royal Infirmary, and its findings are reported in a recent issue of the *British Medical Journal* (4, 586; 1973). The unit had previously used the hexachlorophane preparation Phisohex successfully for many years, but this disinfectant is not entirely satisfactory as it has a fairly narrow range of activity and there is accumulating evidence of the possibility of its toxic absorption. The trials showed that Hibiscrub was just as effective as Phisohex in maintaining low levels of bacteria on the hands during operations and as an added bonus was more pleasant to use and also cheaper.

The members of the Aberdeen team have acted on their findings and now use Hibiscrub as their routine surgical scrub.

Name Dropping

QUEEN'S University, Belfast, is sometimes embarrassed by the 'Queen's' part of its title and often drops the word from its advertising copy. But there is no sinister motive behind this. The true explanation is more mundane. A spokesman for the university said recently that "when our advertisements are classified alphabetically under 'Q' our prospective applicants sometimes get tired before they get to us". This alteration to the name applies only to publications outside Northern Ireland.

At home they stick loyally to the full title.

BRITISH COUNCIL

Looking East

CONSOLIDATION was the keyword in 1972 as far as the British Council was concerned. The council's annual report published recently (available from 65 Davies Street, London W1Y 2AA) emphasises that the purpose of the council has remained unchanged since it was established forty years ago. It is still in existence to "make the life and thought of the British peoples more widely known abroad . . . to enable students from overseas to undertake courses of education or industrial training in the United Kingdom . . . to bring other peoples into closer touch with British ideals and practice in education, industry and government . . . to make available to them the benefits of British contributions to the sciences and to technology . . ."

The latest people to benefit from the attention of the council are the Chinese from the People's Republic. During 1972-73 there was a marked increase in the council's contacts in China and many Chinese came to Britain last year to study English. Recently, the council has, acting as an agent for the British Government, placed sixty Chinese post-

graduates in science, technology and medicine in one-year posts in Britain. These people are mostly between the ages of thirty and forty-five. The first few have already arrived and are in the process of learning English. They will start their scientific work in January.

The council's budget for 1972-73 was £20.51 million, of which £18.98 million was covered by a parliamentary grant. The remainder came from earnings and private donations. For 1973-74 the budget has only increased by a modest £234,000. About 20% to 25% of the budget is spent on science although the accounts do not allow a direct extraction of this sum.

The council at present employs eighty-one scientifically qualified officers but not all of them are in posts directly associated with science. Fifty-seven of them are abroad and twenty-four are in Britain, most of them in London at the head office.

In the past two years the number of science officers in Europe has doubled. Until 1972 the council had science officers in Spain, Italy and Germany. During 1972-73 a science officer was assigned to the Paris office and recently one science officer has been appointed to Scandinavia and another to the Benelux countries.

DEAFNESS

Wiring for Sound

STUDIES are in progress at the Institute of Sound and Vibration Research at the University of Southampton on the possibility of implanting electrodes into the inner ear to restore hearing in cases of deafness where the auditory nerve is undamaged but the cochlea no longer works.

A feasibility study has been carried out for the Medical Research Council (MRC) by Dr A. R. D. Thornton and Mr N. V. Morgan, both members of the institute.

A number of electrode implants have been carried out in the United States. These have only picked up low frequency sounds and have not helped much in the hearing of speech. But lip reading has been made easier.

The Southampton studies will assess the possibility of plugging a number of electrodes into the cochlea so that a fuller range of hearing can be restored. Dr Thornton says that the operation is already possible with existing technology, although many questions have to be answered before it is certain that the technique can be used.

Operations in the United States have been suspended until better devices are available for implantation, and because there are fears that the silvered electrodes could lead to heavy metal poisoning in the brain. The MRC team will

also be examining the possible long term effects of implanting the electrodes in the cochlea as well as the effects of repeatedly stimulating the auditory nerve with an electrode.

If the technique proves to be workable it is estimated that 20% of deaf people could benefit. But it is far from certain that the research will be successful. Dr Thornton says that "even if I had a patient with a good auditory nerve I would do everything in my power to dissuade him from having one of these operations at the present time". Mr Morgan warns that for people who have been deaf for a long time the technique may create as many problems as it solves. Patients will not just wake up and be able to hear. They will have to get used to interpreting the changed speech patterns that they will hear with the aid of the electrodes.

The institute is also about to start work on a programme of hearing conservation with the help of a £13,000 grant for a three-year period from ICI and Amplivox. Under the leadership of Dr Alan Martin the institute intends to examine why the majority of workers in noisy industries refuse to wear protective clothing.

Dr Martin points out that one company spent £18,000 over eighteen months on hearing protection for its employees, most of it on protective clothing, only to find that only 2% of staff were wearing it.

NEWS AND VIEWS

Climatic Change in China over the Past 5,000 Years

"In the fields of the struggle for production and scientific experiment, mankind makes constant progress and nature undergoes constant change."

Now that scientific contacts with China have been re-established, a vast pool of information about historical changes in climate has become available. The quotation from Chairman Mao Tsetung which appears above comes from a paper by Chu Ko-chen, who highlights one facet of the constantly changing face of nature by presenting evidence of how the climate of China has fluctuated over the past 5,000 yr (*Scientia Sinica*, 16, 226; 1973). Western climatologists will no doubt be delighted to have this comprehensive review available, even though the author modestly disclaims it as preliminary work which, while elucidating a few problems, also puts forward a lot of new puzzles. As Chu Ko-chen says, "misinterpretations . . . are unavoidable" when looking at the oldest historical records—but misinterpreted or not, at least the records from China are essentially continuous for the entire 5,000 yr period.

The interval of 5,000 yr falls naturally into four sections:

- The archaeological period, from 3000 to 1100 BC, when there were few written records except those carved on the oracle bones.
- The documental period, from 1100 BC to AD 1400, for which there are written documents but no detailed regional reports.
- The gazetteer period, from AD 1400 to 1900, when many districts kept records of history and geography which contain climatic information.
- The instrumental period, from 1900 onwards, in which detailed meteorological records have been kept.

Even for the earliest of these periods important climatic evidence is available. The oracle bones, which contain many inscriptions praying for rains, provide an important clue; evidence of farming activity, and farming methods, provides another. It seems that since the time of the Yangshao culture, 5,000 yr ago, the northern limit of bamboo has moved south by 3°. This corresponds to a decline in temperature along the lower reaches of the Yellow and Yangtze rivers of about 5° C (on average) for January and some 2° C for the mean annual temperature. Yangshao and Yin-Hsu times, at the earliest period of the 5,000 years studied, seem to have been a climatic optimum in China, when rich subtropical fauna and flora flourished in places like Sian and Anyang. But "as to the existence of elephants in the northern part of China during the neolithic age, it is still a moot question," says Chu Ko-chen.

In some ways, the analysis of evidence from the documental period is the most fascinating. Here, there is no lack of data—the problem lies in interpretation to give a self-consistent picture. The keeping of official records began with the founding of the Chou Dynasty (1066 to 256 BC), with first inscriptions in bronze and later written records in bamboo books. But the official historians were not the only people to leave records, and poets in particu-

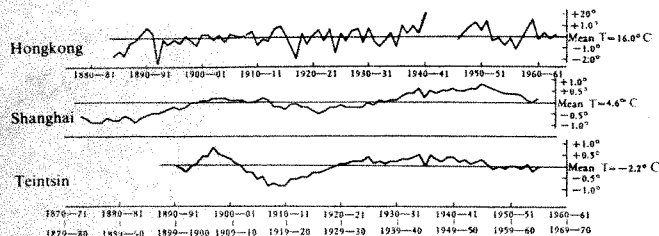
lar have left descriptions of birds and flowers from which evidence of climatic change can be deduced. Certainly, at the beginning of the Chou Dynasty the climate was warm enough to grow bamboo extensively in the Yellow River Valley. But the climate soon deteriorated, and the Han River, a tributary of the Yangtze, froze in 903 and 897 BC. Great droughts followed the freezing, but conditions in the mid-Chou period were rather better. Plum trees, much loved by the Chinese, became common throughout the country, and from about the ninth century BC to the time of Confucius (557 to 479 BC) the Yellow River valley was slightly warmer than it is today. The next cold period began about 200 BC, and in the space of a century there were six very severe winters, with frost and snow occurring in late spring months, and many people froze to death. From the first century BC to the first century AD the climate again recovered, but between AD 155 and 220 attempts to grow oranges in the royal garden at Loyang "failed dismally", even though oranges had been grown in the royal gardens during the Han Dynasty some 300 yr earlier.

The astronomer-poet Chang Heng (AD 78 to 139) had written an ode in which he referred to plentiful orange groves near the "South Capital"—but in AD 225 naval manoeuvres at Kuangling had to be suspended when the Huai River froze, for the first time on record. So the pattern of warm and cold periods continues; it is plausible to argue, for example, that during the 8th and 9th centuries AD temperature and rainfall belts in the eastern part of China were shifted a little north relative to their present day positions, and Chu progresses through the maze of documental evidence up to the 12th century. Then, there was a much more dramatic change in the climate.

In the past few years, climatologists (and even some non-experts) have come to be familiar with the idea of a 'Little Ice Age' which affected Europe and Britain some 500 yr ago, and which may have been at least partly responsible for the loss of Viking colonies in North America and Greenland. But in China, it seems, this little ice age was pronounced in the 12th century, considerably earlier than in the west. Japanese records confirm this; from the 9th century onwards, nobles celebrated the blooming of Japanese cherry trees (a sensitive climatic indicator) and appropriate records were kept until the 19th century. Climatic changes in China and Japan paralleled each other during that millenium. The long cold period lasted effectively from the 10th to the 14th centuries in China, with the severe cold of the 12th century corresponding most closely with the western little ice age. Development and movement of this cold spell can be traced from east to west, since a cold period began in European Russia around 1350, and in central Europe between 1429 and 1465; in England it was during the 16th century that conditions became so serious that they led to the Elizabethan legislation on poverty. Lamb has already pointed out that "the greatest incidence of anomalies moved westward across Europe during the climatic deterioration from 1300 to 1600 and returned to the East

during the recovery from 1700 onwards". Extending this pattern of climatic movement to China and Japan provides one of the most powerful tools yet for climatic research and prediction of future trends.

Records from the gazetteer period provide, among other data, further evidence of this east-west movement of climatic change. Freezing of lakes indicates unusually severe winters, and although this kind of evidence from China and Japan shows that the 17th century had the most severe winters in both countries, in Japan the period of severe freezing started and ended 25 yr before the corresponding period in China. The evidence from the instrumental period seems almost mundane compared with the importance of the historical data, but this shows a pattern of upward and downward swings in temperature, by between 0.5 and 1° C, which is obviously of great significance in predicting future trends, particularly to the farmers (see figure). This kind of swing, with a period of rather more than 40 yr, has been going on for thousands of years, although sometimes obscured by more dramatic changes. Perhaps this is the sort of effect which can be tied to solar activity (see J. W. King, *Nature*, **245**, 443; 1973; and J. Gribbin, *Nature*, in the press), although Chu does point to some difficulties in relating the coldest winters in the 19th century to the pattern of solar variation.



Winter mean temperature (T) for Hongkong (upper curve) and sliding ten-year average of winter mean temperatures for Shanghai and Tientsin.

In summary, beginning 5,000 yr ago: for the first 2,000 yr China was about 2° C warmer than today; then, a series of up and down swings with minima at about 100 BC, AD 400, AD 1200 and AD 1700 and amplitude 1 to 2° C can be traced from the more complete data available. Within each 400 to 800 yr period, smaller cycles of 50 to 100 yr in length can be traced, covering 0.5 to 1.0° C in their variation; for both kinds of cycle, the coldest period begins at the Pacific coast of Asia, moving west as a wave right through to the Atlantic coast of Africa and Europe.

So Europe, following much the same pattern of cyclic variations, usually lagged behind China. Chu argues that this is because both climates are controlled by the Siberian high pressure system, and that fluctuations in this high affect the whole of Eurasia in a consistent pattern. This is a particularly persuasive argument following King's suggestion that solar radiation changes influence the weather through an interaction of energetic particles with the North Atlantic high, which is a counterpart to the Siberian system. Preliminary though this investigation might be, together with work now going on in the west (see *Nature*, **245**, 408; 1973), it emphasises the way in which an understanding of climatic change is beginning to emerge. As Chu points out, this is one field of research where Mao Tsetung's policy of "making the past serve the present", and indeed the future, is particularly apposite. Continued study of ancient climate can undoubtedly lead to better long range forecasting.

Records of the 1973 Eclipse

THE preparations for the remarkable total solar eclipse of June 30, 1973, were described earlier in this column (see *Nature*, **243**, 490; 1973). In this issue appear some of the first results of experiments associated with this event (Beckman, page 411; Beckman and Clucas, page 412; and Koutchmy *et al.*, page 414).

Skies were clear along most of the track of totality, though wind-raised dust spoiled some of the experiments located in the Sahara. But this has not prevented Koutchmy *et al.* from achieving a notable 'first' by their detection of a 100 km s⁻¹ motion of a large filament in the solar corona, about 3 to 5 solar radii out. This the Franco-Russian team achieved by the simple device of comparing photographs taken at two observatories spaced 90 min apart along the Sahara segment of the track of totality. At distances from the Sun of 3 to 5 solar radii the corona still consists essentially of almost fully ionised hydrogen, a hydrogen plasma, in which much of the acceleration of the solar wind is thought to take place. It is feasible that the outward motion of the filament is direct evidence of this acceleration, but more importantly the relatively rapid motion which was observed runs counter to prevalent models of the corona in which large motions on such a short time scale are neglected.

A complementary experiment on board Concorde 001 was designed to search for changes in coronal structure closer to the Sun, within 1.5 solar radii. The detection of such changes becomes feasible because the speed of Concorde 001, Mach 2.05, retards the apparent motion of the Moon to give a ten-fold increase in the duration of the eclipse from 7 to 74 min. A preliminary report (Beckman *et al.*, *Nature*, **246**, 72; 1973) has indicated that this and the other experiments on Concorde 001 went very well. Final results from this group of scientists who have obtained more total eclipse time than most solar scientists get in a lifetime are awaited.

During the supervision of his main experiment on Concorde, Beckman (page 411) recorded the time between the first appearance of the red solar chromosphere and the first appearance of the bright photosphere which marked the end of the slowed down eclipse. Because of this slowing down this simple observation has been turned into an estimate of the thickness of the solar chromosphere that is about twice as accurate as previous ground-based estimates. The chromospheric thickness is notoriously difficult to measure because the relatively faint chromosphere is adjacent to the very bright photosphere and is only about as thick as 0.2% of the solar diameter. The thickness is of importance in any theories of the solar atmosphere because the chromosphere is a major feature of this atmosphere.

A minor puzzle is emerging from experiments designed to detect atmospheric gravity waves in the Earth's atmosphere induced by the eclipse. Such waves differ from the familiar acoustic waves because a term representing the work done by a wave against the Earth's gravitational field is included in the equation of motion. They are important because they represent one of the few plausible mechanisms by which considerable amounts of energy may be transported vertically in the atmosphere above and across the tropopause.

Although the atmospheric gravity waves ...

be always present, the mechanism by which a solar eclipse generates them, though complex, is simple compared with the presumed ongoing processes. An essential feature of this mechanism is the cooling induced at various levels in our atmosphere by the Moon's shadow. Whether one detects the waves is therefore a measure of whether the correct model for solar atmospheric heating is being used and whether the corresponding model for generating the waves is correct.

The puzzle is this: during the eclipse of March 7, 1970, effects observed in the ionosphere and at ground level were construed as evidence of eclipse induced gravity waves. During this year's eclipse such effects seem to be absent (Schödel *et al.*, *Nature*, **245**, 87; 1973; Beckman and Clucas, this issue, page 412).

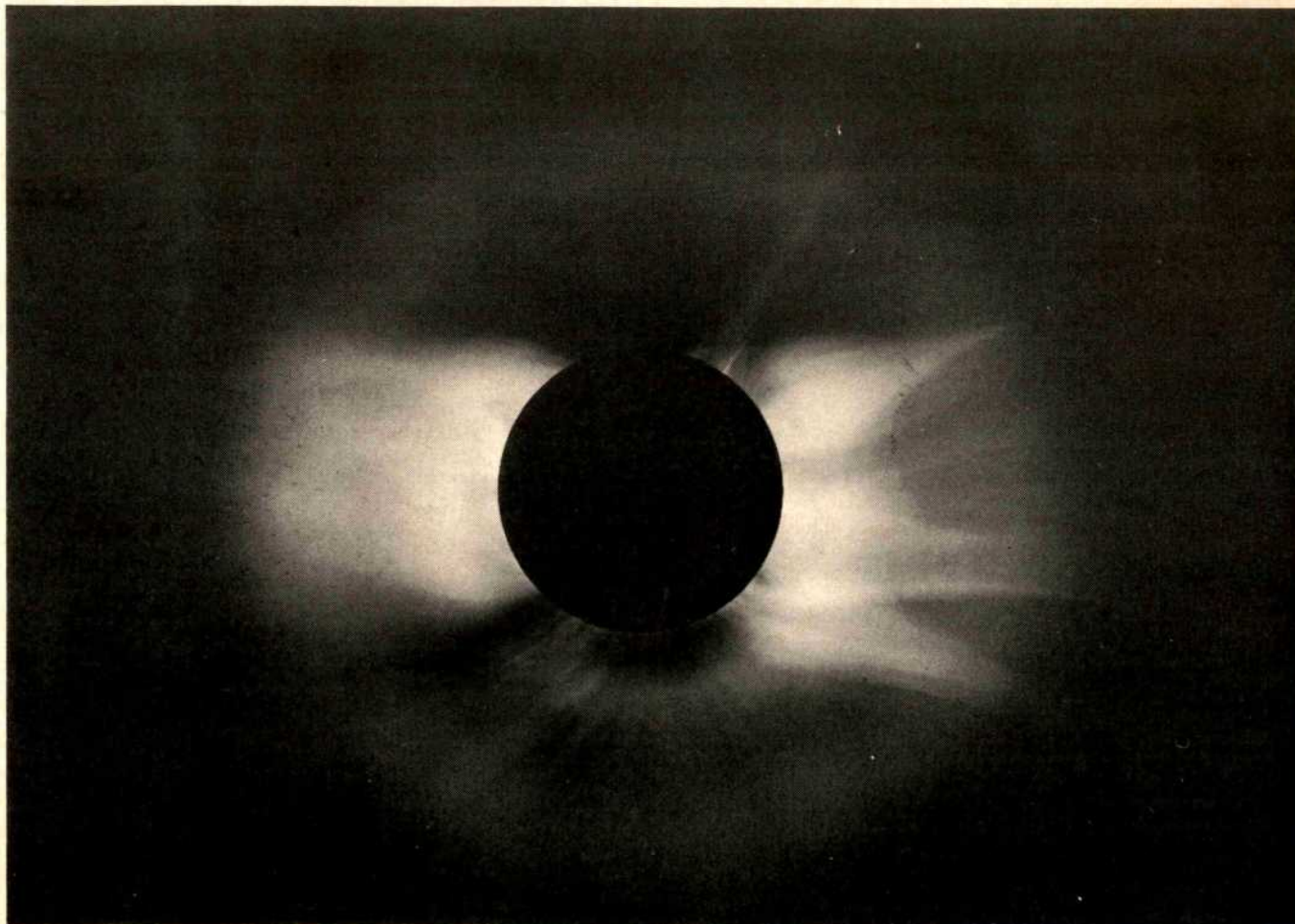
The travelling ionospheric disturbances observed by Davis and da Rosa in 1970 (*Nature*, **226**, 1123; 1970) were convincingly accounted for by Chimonas and Hines (*J. geophys. Res.*, **76**, 7003; 1971) in terms of atmospheric gravity wave generation in the atmospheric ozone, particularly around 45 km altitude. The absence of any evidence for atmospheric gravity waves in the ionosphere in 1973, reported by Schödel *et al.*, could thus be explained in terms of a reduction in atmospheric ozone. This is plausible because the 1970 observations were made north of the equatorial zone in the month (March) in which the amount of ozone is near the annual maximum. By contrast, the 1973 observations were made in the equatorial

zone in June and the amount of ozone is expected to be lower. Moreover, 1970 was close to a peak in the eleven-year sunspot cycle and hence a peak also in solar X-ray and ultraviolet-ray flux. This flux generates ozone. Thus since in 1973 these fluxes are half-way to minimum values the solar cycle is another way to account for the 1973 absence of evidence for gravity waves in the ionosphere.

The ground pressure waves detected in 1970 by Anderson *et al.* (*J. atmos. Sci.*, **29**, 583; 1972) were a hundred times larger than those predicted by Chimonas using the same model that he has used successfully to account for the ionospheric observations. The experimental upper limits placed on the 1973 ground pressure waves are of the order of the theoretical predictions.

It is not certain that the ground pressure waves detected in 1970 were induced by the eclipse but, assuming that they were, then one has to find a way of leaving the ionospheric story untouched while at the same time accounting for the large 1970 effect on ground pressure and an effect in 1973 that is at least 100 times smaller. Hope lies in invoking mechanisms for generating the waves in addition to that based on ozone. Near ground level the absorption by water vapour of infrared radiation re-radiated from the ground can possibly be used to explain the large 1970 effect, but it is not easy to see why this mechanism for generating atmospheric gravity waves was so much less effective in 1973.

B. W. J.



The solar corona photographed by J. Fagot and S. Koutchmy at Moussoro (Chad) at 12–14 h UT on June 30, 1973, with an exposure time of 10 s. An Ektachrome 18 × 24 cm film was used in combination with a 15 cm diameter compensator made by MTO (France). The standard camera focal length 3 m, objective diameter 20 cm, was made by the Institut d'Astrophysique, Paris, and the University of Kiev. Note the background of the Moon seen through the central hole of the compensator. The Moon is not concentric with the Sun, because the observation was made from a point 88 km from the central line of totality. (Copyright, Institut d'Astrophysique, CNRS, Paris.)

Particle Creation in a Big-bang Universe

ALTHOUGH the 'big-bang' models of the Universe were formulated nearly fifty years ago, investigations close to the big-bang events have been few and far between. Physicists have, on the whole, been hesitant about applying their laws in conditions very different from those that operate 'here' and 'now'. One notable exception is the work of George Gamow more than twenty-five years ago about element synthesis during the first few seconds after the big bang. This led to the prediction of the microwave background which was first observed in 1965.

During the few years since this important discovery, cosmologists have become bolder in tackling the big bang. Many authors, like Zeldovich, Sexl, Parker and others, have examined the possibility of particle creation as a gravitational effect in the highly curved and rapidly expanding Universe just after the big bang. An interesting and novel attempt in this direction has recently been made by Audretsch of the Fachbereich Physik der Universität, Konstanz (*Nuovo Cim.*, **B17**, 284; 1973). This work arose partly out of the author's discussions with the relativity groups in London. Audretsch's approach may be briefly described as follows.

In quantum mechanics the propagation of massive spin- $\frac{1}{2}$ particles, like the electron, is described by the Dirac equation. In the flat space of special relativity, such a particle of given mass and momentum can exist in one of four possible states, described by a plane wave. Each state is characterised with spin, which can be $+\frac{1}{2}$ or $-\frac{1}{2}$ and by energy which can be positive or negative (but with the same magnitude). In order to avoid the awkward negative energy solutions Dirac proposed the 'sea' of negative energy particles. This sea is completely filled and is unobservable. A free particle of positive energy can propagate for ever without taking any notice of this sea. If, however, there is an external force acting on it, such as the electromagnetic field, it changes energy. This can lead to a particle from the sea 'jumping up', for example. Such a particle, and the 'hole' it has created in the sea, then

appear as a pair of particles. This is how particle creation from an energy source like radiation is believed to take place.

Audretsch has applied this picture to the expanding Universe and he comes up with certain important differences. When he considers the plane wave solution of the Dirac equation in the expanding Universe, he finds that only in certain special circumstances do the positive and negative energy solutions stay unmixed. The special cases are (1) the particle in question has no mass (a neutrino, for example) and (2) if the particle is massive it is at rest in the cosmological substratum. For a massive moving particle mixing of states must take place. That is if the particle is initially described by a plane wave with positive energy, it will later on also acquire states of negative energy. This curious effect, Audretsch finds, is entirely due to the expansion of the Universe. By analogy with the flat

space picture just described, he concludes that the appearance of negative energy states must be interpreted as particle creation. This is how matter appears in the expanding Universe.

According to Audretsch the effect of expansion is significant for particle creation when the age of the Universe is comparable to the microphysical time scale—when the Universe is only about 10^{-21} s old! This is hardly surprising in a theory which seeks to relate microphysics with cosmology. In this work Audretsch has steered clear of many relevant but complex issues, such as the implications of quantum field theory (this work does not quantise the Dirac field), the effects of quantising the space-time geometry, the implications of the negative energy sea for Einstein's field equations and so on. No doubt such problems will keep theoretical big-bang cosmologists busy in years to come.

J. V. N.

DEMOGRAPHY

Conflicting Population Reports

from our Demography Correspondent

ONE of the professed aims of the United Nations World Population Year, 1974, is improvement of knowledge of population trends, particularly in the Third World. The recent history of population projections for the United Kingdom, where population statistics are among the world's best, in terms of range and quality, indicates that this will not be easy and the conflicting findings of two recently published studies give no basis for supposing that the situation is improving in Britain.

A set of official projections (*Population Projections*, No. 3, 1972–2012, HMSO, London; 1973) suggests a population of just under 58 million for England and Wales by the year 2011, a rise of about 9 million over present numbers. By contrast Gilje and Gould of the Greater London Council Intelligence Unit (*Q. Bull.*, No. 24; September 1973) suggest a possible population of about 50 million for the same date, which is only a fractional increase over the present figure. The team of GLC researchers has a very good record of population studies and the projection methods of the two reports are broadly similar. How then can such conflicting reports result?

The answer is that the assumptions on future fertility patterns differ crucially. Both reports use the same mortality and migration assumptions and, though some demographers might argue the future mortality decline assumptions are optimistic, changes in this factor during the projection period are likely to be minimal.

Fertility patterns result from a complex of economic and social factors affecting the decisions of individuals not merely on one matter but several—principally age at marriage, desired family size and the spacing of births in relation to marriage and preceding births. To predict future changes in each of these elements demands the prediction of future patterns of economic and social factors which influence them. This is the familiar problem of an intricate set of interdependencies and feedback relationships. Economists and resource planners see population estimates as basic inputs for their studies of future trends but demographers equally require these projections to make their fertility assumptions.

The population increase suggested in the official projections stems from the assumption that mean completed family

size will stay at about 2.33 and that the decline in births which has occurred since 1964 is a result of birth postponement rather than a decline in completed family size. Support for this assumption comes from replies to questions on intended family size in the 1971 *General Household Survey* (HMSO, London; 1973) but, as the GLC study points out, intended behaviour may not be a good indicator of actual behaviour in this case and replies may reflect spontaneous feelings at interview time rather than firm family size plans.

The authors of the GLC report argue that the fall in births is not a temporary feature at all but a permanent one from a decline in completed family size and an increase in the spacing between births. To support this assumption they cite the way couples who wish to postpone parenthood can do so effectively with modern contraceptives and several reasons which may be encouraging more couples to do this, including the desire of wives to have careers and attaching greater importance to material well-being than family rearing. Against the official projection's assumptions that births are merely being postponed, Gilje and Gould put forward the novel point that the 'appropriate' age range for having a family is socially defined and that some of the couples who may intentionally be postponing births will pass the upper limit of the range without ever achieving their originally intended family size.

The zero growth projection produced by the GLC team is one of two they have produced, on differing fertility assumptions. The other gives a 2011 population of about 53 million, still 5 million below the official figure. None of these three figures can be said to be any more 'accurate' than the other predictions.

At present, Britain is in a transition period of fertility behaviour, contributing at least partially to the differences. Only when the transition ends and the patterns stabilise will the range of alternative assumptions on future fertility behaviour be narrowed.

GEOPOLITICS

Forensic Seismology

from our Geomagnetism Correspondent

"I REMEMBER, when our whole island was shaken with an earthquake some years ago, there was an impudent mountebank who sold pills which (as he told the country people) were very good against an earthquake". As the multi-million dollar industry purveying nostrums for the common cold indicates, the sort of quackery recorded by Joseph Addison in *The Tatler* of about 250 years ago persists to this day, albeit in a form more appropriate to a

supposedly more sophisticated market. Of course, it is hard to imagine that many people today would expect any problem associated with earthquakes to be resolved quite so easily, although, as Dr H. I. S. Thirlaway pointed out some time ago in the Tenth Harold Jeffreys Lecture, some politicians of the early 1960s came very close to it in supposing that there might be a ready-made scientific pill to cure the seismic malady of the day—the headaches induced by the inability to distinguish between earthquakes and underground explosions at a distance. Whether those same politicians ever reversed Addison's indignation and privately berated the seismologists as charlatans for not being able to come up with an appropriate medicine bottle has, not surprisingly, gone unrecorded. At any rate, in public they blamed not the scientists but the science, bandying about such phrases as 'Stone Age' and making invidious comparisons with the state of the more trendy sciences of nuclear physics and space research.

With the publication of Thirlaway's lecture (*Q. Jl R. Astr. Soc.*, **14**, 197; 1973), one is again able to savour the retrospective delights of those early days of treaty making, when one optimistically assumed that what was to become the limited Test Ban Treaty of 1963 could be converted into a comprehensive agreement by rapidly pulling the right pill out of the doctor's hat. This is, of course, the field that Thirlaway himself has christened "forensic seismology". A minor diversion to the dictionary is required here, revealing that 'forensic' derives from the Latin *forensis* for forum or market place—a formal definition which perhaps does too little to emphasise the element of argument implied by the modern adjective. In any event the intended analogy with forensic medicine, or (that dictionary again) "the application of (medical) knowledge to the elucidation of doubtful questions", is perfectly clear and suggests that the experiences of the medicine men of the late eighteenth century might have contained some lessons for the seismologists of the late 1950s who found themselves confronted with scientifically illiterate politicians anxious to politicise science to save mankind.

Consider with Thirlaway, for instance, the example of one John Hunter, a medical man of some repute who was persuaded to give evidence in that capacity in the case of *Rex versus Dunellan* at the Warwick Assizes of 1781. The aforementioned and unfortunate Dunellan stood accused of the crime of poisoning by laurel water, and his prospects were not particularly bright when Hunter was called to appear as an 'expert' witness for the prosecution. Were the described symptoms

ASTRONOMY

Lockyer's Telescope



SIR NORMAN LOCKYER'S 6½ inch Cooke refractor has found a new home only 80 miles from the observatory which he founded at Sidmouth in his declining years (see *Nature*, **240**, 176; 1972). Early in 1972 the Exeter Astronomical Society started building a 15-foot-diameter dome to house Lockyer's historic instrument, and on August 11 this year the inauguration of the completed project was performed by Professor G. K. T. Conn, Director of the Norman Lockyer Observatory.

The telescope is that with which Lockyer made his spectroscopic analyses of the Sun, culminating in his discovery of helium. One hundred years since Lockyer made his first drawings of Mars the instrument is being used for drawings of the present opposition of that planet by the amateur members of the Exeter Astronomical Society.

An extensive programme of observations, including lunar and planetary studies, is in progress by members of the society, and soon photographic work will be started with the installation of an electric equatorial drive.

consistent with death by laurel water or were they not? the court wanted to know of Hunter. The poor Hunter did not know. "I do not mean to equivocate," he said, "but when I tell the sentiments of my own mind, what I feel at the time, I can give nothing decisive."

Nor, according to Thirlaway, could the scientists on the technical working group of the Geneva Conference of the Discontinuance of Nuclear Weapon Tests who began work on October 31, 1958. They found themselves in much the same dilemma as John Hunter; and, like John Hunter, they discovered too late their lack of clothes. Of course, Hunter and the early history of forensic medicine were hardly uppermost in their minds; nothing had been learned from history (a common enough failing)—neither from the vast case history of medico-legal activity, nor, Thirlaway might have added, from the equally vast precedent involving the many Earth scientists who had been called upon to

give evidence in legal disputes centred on such geological phenomena as metaliferous lodes with an unfortunate tendency to stray at depth onto a neighbouring claim. The seismologists who gathered in 1958 to do their bit in preventing man from blowing himself up simply did not possess the knowledge assumed of them. Fifteen years later they still do not possess the knowledge needed to monitor underground explosions faultlessly; but they do have a greater knowledge of themselves. Indeed, in summing up the failings of the earlier years, Thirlaway could well have written an appropriately grave epigram: "We were persuaded to appear as witnesses to testify about what we did not know".

But although the embarrassing lack of knowledge where knowledge was (perhaps naively) expected was the most important single difficulty that Thirlaway and his colleagues had to face, matters were hardly helped by the circumstances in which this deficiency became clear. The seismologists who were precipitated into science politics in the late 1950s hardly surprisingly felt themselves to be in an alien environment. "We did not enjoy the public gaze in which often we had to work; we had little or no experience in hand-

ling the news media. . . . We were not careful enough to separate fact from opinion and comment for the benefit of our officials; we did not give sufficiently direct answers to simple questions; we filled our answers with technical terms and jargon as though addressing professional societies rather than State officials. . . ." In short, insofar as the politics of science was concerned, the seismologists as well as the science were in the Stone Age; they were, as Thirlaway admits, innocents abroad in the tough political arena.

In his now-published lecture Thirlaway also admits much more. But it is nearly Christmas, the season of goodwill and charity; and I shall not act against traditional precepts by spoiling a good story completely. Thirlaway's confessions need to be read in their full form without the aid of an interpreter. But how full is full? Surely there could be more? Could Thirlaway be persuaded to testify about what he does know to the length of a book? To take the point quite seriously, the early (and later) days of forensic seismology form an important, though neglected, part of the history of the interactions between science and politics. It would be a pity if the full story were to be lost.

INSECT EYE

Duality of Vision

from our Insect Physiology Correspondent

It has long been held that separate photopic and scotopic mechanisms for day and night vision, such as are well recognised in vertebrates, do not exist in insects. The most familiar effect of the duality of human vision is the so-called 'Purkinje shift'—a change in the wavelength to which the eye is most sensitive as the light becomes more dim. Such a change was demonstrated in *Drosophila* many years ago by Fingerhman and Brown, but the tendency has been to find other explanations for this observation. In recent years it has been shown by Goldsmith *et al.* in flies, and confirmed by Carlson in moths, that prolonged vitamin deficiency, extending over many generations, induces a loss in visual sensitivity which affects the longer wavelengths more than the shorter wavelengths and the ultraviolet; a result which is reminiscent of 'night blindness' in man; and Cozens found that dark adaptation in insects involved a two step process, not related to pigment migration, suggesting the separate existence of photopic and scotopic mechanisms.

In 1972 S. L. Swihart, while studying the waveform of the electroretinogram (ERG) of diurnal butterflies and moths,

found that different components responded differently to drugs, inorganic ions and the like, and differed from each other in regard to flicker fusion frequency, latency and spectral sensitivity, as well as to light adaptation. All this strongly suggested the existence of retinal duality. Swihart (*J. Insect Physiol.*, **19**, 2035; 1973) has now investigated this question systematically, applying the sort of tests from which the existence of the dual system of vertebrates has been inferred.

Swihart has shown (1) that there is a change in the flicker fusion frequencies on adaptation to night vision; (2) that there is a change in the slope of the curve of "stimulus energy vs response" and, as was to be expected, the photopic receptors have a higher threshold and lesser slope than the scotopic; (3) there is a break in the curve of activity in visual interneurons as the energy of the stimulus is steadily increased; and (4) the electric potentials recorded as evidence in the ERG are already operating in the pre-emergent (pharate) adult butterfly and are therefore unlikely to be originating in neural structures.

Finally, Swihart has formulated a theoretical model of the insect eye, based on the duality concept, which can reproduce quantitatively the changes obtained experimentally in the ERG records in respect to flicker, in both waveform and amplitude.

POPULATION ECOLOGY

Vole Demography

from our Animal Ecology Correspondent

THE regular occurrence of sunspots, the cycle of ozone content of the atmosphere, the quality of vegetation and the activities of predators have variously been held up as the explanation of rodent population cycles. There seems a need among ecologists to look for just one factor as the sole directive agent.

It is therefore refreshing to read Lidiker's paper on the regulation of an island population of *Microtus californicus* in which no single controlling factor emerges with more importance than any other (*Ecol. Monogr.*, **43**, 271; 1973). Lidiker studied the voles on Brooks Island in San Francisco Bay from their arrival there in 1958 until 1971—a period of thirteen years. Such long-term studies are invaluable and regrettably rare, but infinitely more useful than the short-term studies upon which much ecological creed is built.

A few voles reached Brooks Island from a neighbouring islet 230 yards away in the summer of 1958 and for the following 2 years the population increased very rapidly. During the study a variety of censusing techniques were used, but most of the sampling was carried out on a trapping grid of between 0.08 ha and 0.49 ha. After the initial 2 years of rapid increase the population settled down to a regular pattern of numerical change. Reproduction started about 2 months after the start of the rainy season (November); a period of high corpus luteum production and large litter sizes began about 3 months after the start of the rains; the build-up to peak numbers did not occur until very late in the breeding season; body growth was halted for about 5 months from the start of the dry season; moulting occurred in two discrete seasons, May to June and September to November; and, finally, winter densities alternated high and low. The 2 years of colonisation were typified by numerous births within a month of the rains starting, a rapid growth of the population early in the breeding season, and a continuous high density showing no winter decline. Clearly then some factors operated during the 11 years of 'stability' which did not operate in the colonisation years.

The pattern of wet and dry seasons has an important, but not altogether understood, influence on dynamic processes. The vegetation responds within 5 days to the start of the rains, yet the rodent population takes 2 months. Lidiker thinks that those individuals that have passed the dry season, usually at high density, suffer some kind of physiological damage. The marked population increase starts when their few offspring themselves start to breed. The influence of physio-

logical damage on rodent population dynamics has been suggested by Chitty in his studies on *M. agrestis* (*Phil. Trans. R. Soc.*, **B236**, 505; 1952). Lidiker considers that nutritional defects of the vegetation did not cause the delay, since young males increase in weight and recommence growth long before other age and sex groups.

The alternation of overwintering numbers seems to be a normal oscillatory process. High winter numbers damage the habitat and induce low dry seasonal survival the following year and also low winter numbers. This reduction in grazing pressure allows the forage to recover and so better survival is seen in the third year.

When all the many population data Lidiker has amassed are examined it is clear that no single factor emerges as the dominant controlling influence. Lidiker lists six factors—both density dependent and density independent—which interact to provide control. If any one factor must be singled out as having a more direct effect on the population than any other, then it must be the pattern of rainfall.

The regular pattern of population dynamics could be modified into the 3 or 4 year cyclical pattern (for example, Krebs, *Tech. Pap. Arct. Inst. N. Am.*, No. 15; 1964) regarded as 'normal' for small rodents by (1) the action of predators responding to the build-up by increased breeding (there were no predators on Brooks Island); (2) delay in the onset of breeding due to physiological damage after a 'crash'; (3) emigration occurring; and (4) a rapid build-up when (1), (2) and (3) have all had their effects.

The Brooks Island study shows that the dynamic pattern is neither controlled exclusively by extraterrestrial phenomena, interpopulation phenomena nor intrapopulation phenomena, but by a complex interaction of factors. Lidiker has done rodent population biology a real service by pointing out that at least one natural population behaves according to the complex dictates of the whole environment of which it is a part.

PURPLE MEMBRANE

Light-driven Pump?

from a Correspondent

THE purple membrane is a specialised area of the cell membrane of the bacterium *Halobacterium halobium*. Recently the vivid colour of this membrane fragment was shown to be due to a complex of protein with retinal, the aldehyde derivative of vitamin A. The protein is the only species in the membrane and is packed in a crystalline array (Oesterhelt and Stoekenius, *Nature new Biol.*, **233**, 149; 1971; Blaurock and Stoekenius, *ibid.* 152). Since retinal also gives the

visual pigments their characteristic colours, it was suggested that the purple membrane might be a photoreceptor. Oesterhelt and Stoekenius, however, now summarise experiments done by themselves and several coworkers which lead them to suggest that the membrane pumps protons out of the bacterial cell by using light energy. The resulting gradient may be a source of metabolic energy (*Proc. natn. Acad. Sci., U.S.A.*, **70**, 2853; 1973).

The purple membrane forms in the cell envelope if a growing culture is aerated with oxygen-poor air, whereas if the culture is vigorously aerated with normal air the membrane fails to form in significant amounts. If aeration of a growing culture is stopped altogether, the total cell protein fails to increase further but the purple membrane increases fifty times. Illuminating an oxygen-poor culture can increase the proportion of the purple membrane to half the total membrane area. Moreover, growing cells from a late-log phase culture use less oxygen when illuminated than when in the dark; one less oxygen atom is consumed for about every thirty photons absorbed by the purple membrane in the cells (*FEBS Lett.*, **36**, 72; 1973). Starved cells, which consume reduced amounts of oxygen, similarly use even less oxygen while in the

light. These results taken together indicate that the purple membrane compensates for a lack of oxygen. By what means?

When isolated purple membrane fragments in an unbuffered medium are exposed to a bright light, the pH drops, and it recovers the original value in the dark. Correspondingly, a 'bleached' form ($\lambda_{\max}=412\text{ m}\mu$) of the purple protein is found during the illumination, and the normal form ($\lambda_{\max}=568\text{ m}\mu$) is recovered in the dark. The time courses for bleaching and recovery are the same as for the pH effects (*Eur. J. Biochem.*, **37**, 316; 1973). The starved cells similarly make the medium more acid as long as the light is on, and anaerobic cells also cause a net drop in pH in the light. The net increase in proton concentration when whole cells are illuminated is said to be at least twenty times that for the same amount of purple membrane after isolation. It is therefore suggested that the membrane protein may operate in a cycle, repeatedly picking up a proton from within the cell and ejecting it when light is absorbed. Thus the purple protein may be the first membrane pump to be isolated.

The authors refer to Mitchell's chemiosmotic theory (*J. Bioenergetics*, **3**, 5; 1972) and suggest that a resulting electrical potential across the membrane is

FOOD BIOCHEMISTRY

Fragrance of Bread

from our Soviet Correspondent

AT present approximately 100 compounds are known to contribute to the characteristic fragrance of baking bread. These include, in particular, carbonyl compounds such as furfural and oxymethylfurfural, and also fermentation products such as organic acids, complex ethers, acetaldehyde.

A recent study, carried out by a team from the "A. N. Bakh" Institute of Biochemistry of the Soviet Academy of Sciences and the All-Union Research Institute of the Bread Industry, studied how the formation of these aroma-producing substances depends on the thermal and time regimes of baking. It was found (see Kretovich *et al.*, *Prikladnaya Biokhimiya i Mikrobiologiya*, **9**, 5; 1973) that the fragrance is essentially due to chemical changes within the crust, little contribution being made by the soft crumb, the chemical composition of which remains relatively stable. The decisive role in the formation and accumulation of carbonyl compounds within the crust is played by the formation of melanoidine during the baking process.

This process falls into three stages. During the first stage, which lasts for about 25% of the baking time, the

temperature of the crust rises from 20 to 90–100° C, while the temperature of the crumb rises to 38° C. During this stage there is a certain loss of volatile carbonyl compounds, notably acetylene, from the crust.

In the second stage (the middle 50% of the baking time), the crust temperature rises to 130–140° C and intensive melanoidine formation occurs, accompanied by a build-up of carbonyl compounds in the crust as a result of melanoidine reactions. In particular, the furfural content of the crust, especially the top crust, increases, and the loaf assumes the characteristic coloration of well-baked bread. At the same time, the content of amino acids (aspartic and glutamic acids, threonine, tryptophan, methionine, valine and leucine) decreases throughout the whole loaf, the decrease being most marked in the crust, due to the consumption of these amino acids in the processes. During the second stage, the rate of reaction depends essentially on the crust temperature.

The third period (the last 25% of baking time) is characterised by an intensive build-up in the crust of compounds with bisulphite bonds, acetaldehyde and furfural. During this period, the temperature may fall slightly, and the chemical reactions, although similar to those of the second stage, now take place at constant rate.

used to synthesise ATP. When oxygen, and not light, is available the oxygen is used instead of the light to pump protons and so create the necessary potential.

An experimental observation on the anaerobic cells which is not so readily explained is a repeatable fast rise in pH when the light is first turned on. The rise is followed by a larger, slower fall leading to the net drop in pH already described. Oosterhelt and Stoerkenius suggest an initial influx of protons already forming a gradient across the cell membrane before the light is turned on. Adding an uncoupler causes the pH to rise, and the light effect is said to be abolished.

These results, although interesting in themselves, may also stimulate work on the visual pigments the function of which, beyond absorbing light, is still uncertain.

INSECTICIDES

Toxic to Cuticle

from a Correspondent

CHEMICALS have long been used in the control of insects of agricultural, veterinary and public health importance, but as their use has increased so resistance to the compounds has built up to the extent where some chemical pesticides now no longer provide economic and safe control. The use of other pesticides, notably some organochlorine compounds, has been severely restricted on account of their propensity for accumulation in food chains and consequently the pollution of the environment. A new class of insecticidal agents has recently been encountered which, apart from exhibiting a novel mode of action, also promises to be relatively innocuous as far as damage to the environment is concerned.

The laboratory evaluation of two members of this class of compounds 1-(4-chlorophenyl)-3-(2,6-dichlorobenzoyl) urea (designated PH 60-38) and 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl) urea (designated PH 60-40) is presented by Mulder and Gijswijt in a recent issue of *Pesticide Science* (4, 737; 1973). The toxicity of the two compounds has been evaluated in mice, rats and rabbits, where oral, intraperitoneal and dermal administration produces no toxic symptoms, and lethal doses are extremely high.

Several orders of insects were represented in the studies; lepidopterous and dipterous species proved the most susceptible. Insecticidal activity is manifested in the failure of larvae to moult or pupate so that the insect ultimately dies. PH 60-38 and PH 60-40 have so far shown no action on either the fecundity or on the viability of the eggs or larvae of treated adults. Toxicity to

larvae is evident only when taken orally. If the compounds are applied topically to the larvae, or applied to the nutrient solution of the food plant (some chemical insecticides are absorbed, transported and distributed throughout the plant, so that much of it becomes toxic to its insect predators), no toxic effects are elicited in the larvae.

Failure of the larvae to moult or pupate adequately is due to the disturbance in deposition of endocuticle caused by treatment. If the compounds are applied more than 24 h before a moult, no new endocuticle is laid down; and if treated shortly after a moult, strengthening of the endocuticle is prevented. Larvae treated before pupation either do not survive pupation, or emerge as abnormal adults. Treatment therefore results in the formation of a delicate cuticle which is unable to resist internal pressures, and larvae fail to extricate themselves completely from the exuviae at ecdysis. Death largely becomes apparent through loss of moisture, blackening, immobility, and strongly degenerated adipose tissue. So the compounds can be expected to be relatively benign and relatively specific in the right situation.

Development of biological means for controlling insects is providing more selective and non-persistent forms of control; but control of insects by biological means alone is unlikely to suffice in all instances. It is in integrated control programmes, where the blending of biological and chemical means of control ensures the use of the best features of each component, that the newly discovered action of this series of compounds could prove invaluable.

The compounds will be relatively selective in that they will act only on those insects actually eating the outer surfaces of plants. One drawback is that good coverage of plants with the pesticides must be achieved and is important for ensuring the effectiveness of compounds which act only after ingestion by pests. One other drawback is that treated larvae will continue to survive and destruct normally until the next moult, so that a certain amount of plant damage is inevitable. The efficiency of the insecticides will obviously depend on treatment of early instar stages.

ANIMAL PHYSIOLOGY

Bird Bodily Functions

from a Correspondent

THE study of avian physiology as a subject in its own right has blossomed in recent years and many well known enigmas have been solved. Progress has been made because proper physiological studies are being carried out, as speakers at a Zoological Society of London symposium on "Advances in

VIRUSES

Pox on the Elephant



THIS extraordinary photograph has been taken by Drs S. S. Kalter, R. J. Helmke and R. L. Heberling of the Southwest Foundation for Research and Education, Texas.

They write: The list of poxviruses grows larger each year with the isolation of serologically distinct entities, all with the biological characteristics of the poxvirus group, from the multitude of animal species. Andrews and Pereira (*Viruses of Vertebrates*, third ed., Williams and Wilkins, Baltimore, 1973) as well as Wildy (*Classification and Nomenclature of Viruses*, Monographs in Virology, 5, Karger, Basle, 1971) provide detailed information on the structure and other properties of the poxviruses. Electron micrographs depict the poxviruses as "brick-shape or ovoid complex particles" from such animal species as rhinoceros, buffalo, camel and so on. We have recently observed a configuration that makes us suspect that the elephant may also harbour a poxvirus.

Avian Physiology" (November 22-23) made clear. Thus the bodily functions of birds are no longer simply the subject of brief excursions by mammalian physiologists in search of 'models', zoologists seeking comparative information or poultry scientists requiring physiological background to husbandry problems. As several speakers implied, however, some workers on non-mammalian vertebrates still do not attempt to attain the high standards set by mammalian physiologists. A point made by M. J. Purves (University of Bristol), who dealt with cardiovascular control, was that the most valuable information is usually the most difficult to obtain.

There have been no more spectacular advances made than in avian respiration; these were dealt with by K. Schmidt-Nielsen who, with colleagues at Duke University, North Carolina, and one ostrich, was largely responsible for discovering how the respiratory mechanism of birds works.

different from that of mammals, operates. V. A. Tucker, also from Duke, explained the energetics of bird flight—a field in which a knowledge of aerodynamics and physiology combined with excellent experimentation involving trained birds in a wind-tunnel has led to a real understanding. E. Skadhauge (University of Copenhagen) who was not only responsible for demonstrating unequivocally that salts and water from urine can be reabsorbed in the cloaca and rectum, but also for describing the transport mechanisms involved, has profitably extended his work to study the physiological adaptations of this process in relation to habitat.

Much of the work presented was of fundamental importance to an understanding of animal organisation, for example, M. Peaker (ARC Institute of Animal Physiology, Babraham) presented evidence that the osmoreceptors which control the salt glands in marine birds are located in or near the heart, and an obvious question is whether similar receptors monitor salt and water balance in other vertebrates. A field in which avian studies have been of great fundamental value and ahead of mammalian studies is the photoperiodic control of reproduction. Therefore the control of reproductive cycles and reproductive behaviour occupied a large part of the symposium. B. K. Follett (University College of North Wales) described experiments done in collaboration with D. S. Farner (who led the final discussion) and colleagues at the University of Washington, Seattle, to test the Bünning hypothesis of biological time measurement; such a test would not have been possible had it not been for the development of a sensitive radio-immunoassay for avian luteinising hormone. Environmental factors were not overlooked and R. K. Murtton (Monks Wood Experimental Station) explained the way in which ecological adaptation will have to be explained in terms of control mechanisms. But natural environmental factors were not the only type considered and A. S. Cooke, also from Monks Wood, produced clear evidence that some pesticides do have a serious effect on an important reproductive process—formation of the egg shell.

Malcolm Peaker, who organised the symposium for the Zoological Society, explained that the programme had been arranged to cover avian physiology in its widest sense and to bring together those working on domesticated birds, as a part of poultry research, and those working on wild species. Thus this probably unique occasion for British ornithological science attracted a large audience with diverse basic interests, from field ornithology to neurophysiology and aeronautics to animal be-

DRUG RESISTANCE

Bacterial Ingenuity

THE resistance to penicillin shown by many bacteria is in general mediated by a variety of penicillinases (β lactamases) which break the lactam ring of penicillin rendering it inactive. Semi-synthetic penicillins, such as methicillin and carbenicillin, have altered side chains making them far less sensitive to penicillinase action. The bacteria, as usual, have proved equal to the challenge.

In 1961, strains of *Staphylococcus aureus* resistant to methicillin appeared (Jevons, *Br. med. J.*, 1, 124; 1961) only a year after introduction of the drug. On investigation, this resistance did not seem to be mediated by the appropriate penicillinase (methicillinase) (Seligman, *Nature*, 209, 994; 1966).

A component of the resistance to carbenicillin and other penicillins shown by another important wound pathogen, *Pseudomonas aeruginosa* carrying the R factor RP1 (Lowbury *et al.*, *Lancet*, ii, 448; 1969), has now also been conclusively demonstrated not to involve a β lactamase (Curtis *et al.*, *J. gen. Microbiol.*, 79, 163; 1973). The β lactamase (IIIa) specified by this R factor hydrolyses carbenicillin relatively poorly, hardly sufficiently to account for the more than 1,000 times greater resistance shown by these strains. The Bristol group of Curtis *et al.* have now produced a mutant R factor which no

longer codes for the β lactamase but still confers appreciable resistance to carbenicillin and the other penicillins. Resistance to the other antibiotics specified by the R factor remained unchanged.

The mutant plasmid could not be reverted to β lactamase production by further nitrosoguanidine treatment and no spontaneous mutants have been obtained, so it is probable that the β lactamase genes have been deleted. This relatively high level of residual resistance is not due to a chromosomal gene as it disappears when the cells are cured of the plasmid by dodecyl sulphate treatment, neither is it due to a change in the levels of penicillinase Ia production by the plasmid-less cell.

The mutant R factor has been transferred to *Escherichia coli* K12 in which it also expresses a similar resistance pattern.

Penicillin resistance mediated by penicillinases was relatively straightforward to overcome by building new semi-synthetic penicillins, but even when the basis of this new type of resistance is uncovered it may prove difficult to circumvent, as it is much more likely to be due to structural and permeability changes in the cell itself. Methicillin-resistant *Staphylococcus aureus* and carbenicillin-resistant *Pseudomonas aeruginosa* now represent a significant problem in the management of infected wounds.

Pole Tide in the North Sea-Baltic Area

As Lord Kelvin pointed out in 1876, a wobble of the Earth will induce an oceanic tide. In the case of the Chandler wobble, now known to have a period of about 14 months, the induced tide (pole tide) has a calculated equilibrium amplitude of only about 0.5 cm, but is important because, if really equilibrium in form, it will lengthen the period of the wobble by about a month compared with the period for an Earth without oceans. Moreover, the existence of such a pole tide raises the possibility that the oceans may be a primary sink for the wobble energy; and in so far as excitation and decay are related problems, any information on modes of dissipation could throw light on the vexed question of the excitation mechanism of the Chandler wobble.

Measurement of the pole tide is difficult because of the high background noise in sea level, and so reported determinations are few. The most successful result was obtained many years ago by Haubrich and Munk (*J. geophys. Res.*, 64, 2373; 1959), who found a fairly prominent peak in the sea level spectrum at about 0.84 cycles a year, corresponding to a period of 1.19 yr (that is, about 14 months). Since then, however, the

problem has attracted little attention except that data published by Maksimov and Karklin (*Dokl. Acad. Nauk SSSR*, 161, 9; 1965) suggest a larger than equilibrium pole tide in the Baltic.

In *Nature Physical Science* next Monday (December 17), Miller and Wunsch report a further attempt to measure the pole tide, this time based on all available sea level records of more than 25 yr duration published by the Association d'Océanographie Physique. Most of the examined records were ambiguous; in most cases the pole tide did not rise above the background, and where it did it was weak. For records from the North Sea-Baltic area, however, the search was more successful, the pole tide being clearly visible at a frequency of 0.84 cycles a year. Moreover, Miller and Wunsch have also been able to show that there are systematic variations in the amplitude of the tide, from 0.7 cm at the southern end of the Netherlands coast to 1.8 cm at the northern end. In general, amplitudes rise markedly going eastwards from the North Sea into the Baltic and the Gulf of Bothnia, although the values in the constricted waters of the Kattegat are much lower than the general trend.

METEOROLOGY

Solar Activity and the Weather

from a Correspondent

A SYMPOSIUM on "Possible Relationships Between Solar Activity and Meteorological Phenomena" was held at the Goddard Space Flight Center (GSFC) on November 7-8, sponsored by NASA, in cooperation with the University Corporation for Atmospheric Research (UCAR) and the American Meteorological Society. In his welcome and opening remarks, J. C. Fletcher (NASA) dedicated the symposium to C. G. Abbot for his pre-eminent pioneering work in the measurement of the solar constant and the search for solar-meteorological relationships. Dr Abbot, who in 1972 celebrated his one hundredth birthday, was present in the audience.

In the two opening papers W. O. Roberts (UCAR) and J. Wilcox (Stanford University) reviewed some of the statistical evidence to suggest a meteorological and climatic response to variations in solar activity. The statistical evidence presented includes:

- (1) The recurrence of droughts in the high plains of the United States related to the double sunspot cycle of 22 yr.
- (2) An increase in meridional circulations and blocking patterns at high and intermediate latitudes, especially in winter, generally related to high solar activity.
- (3) Glacier advances and other indicators of cold climate in late glacial and post-glacial time occurred during intervals of weak solar activity, and a similar percentage of glacier recessions and warm climate indicators occurred with high solar activity.
- (4) In some regions of the globe the atmospheric pressure increases after geomagnetic storms, whereas in other places the pressure decreases. The reaction time is about 3 d and tends to increase with decreasing latitude.
- (5) High latitudes show higher average pressures at sunspot maximum than at minimum and at high solar activity there is a mass displacement of air toward high latitudes.
- (6) Developing 300 mbar low pressure trough systems entering or forming in the Gulf of Alaska 2 to 4 d after a sharp rise in geomagnetic activity tend to be larger than average size, and the vorticity area index of these trough systems reaches a maximum about 1 d after the passing of a solar magnetic sector boundary, followed by an increase of magnitude approximately 10% during the next 2 or 3 d.
- (7) The mean change in height of atmospheric constant pressure levels during the first 24 h after a flare is greater than

may be expected from mere random fluctuations in height.

(8) Significant increases in westerly winds at the 700 mbar level in the longitude belt from 90° W to 180° occur ~3 or 4 d after magnetic storms.

(9) Thunderstorm activity has been correlated with the Earth's position in a solar magnetic sector and solar hydrogen- α flare activity.

A. J. Dessler (Rice University) discussed some problems in coupling solar activity to meteorological responses since most geophysical phenomena have a high intrinsic noise level and there is no acceptable mechanism to help organise the data into a manageable search. The energy provided by meteorological phenomena is (essentially) entirely provided by sunlight. The solar constant is about 10^6 erg cm⁻² s⁻¹. The available energy flux to the atmosphere of the solar wind and the interplanetary magnetic field for undisturbed conditions is less than one millionth of that of the solar constant, and the meteorological response, related to solar activity energy variations, of less than 0.1 to at most 10^3 erg cm⁻² s⁻¹. So a 'trigger mechanism' is envisioned since brute force will not work. Dessler discussed the hypothesis of C. O. Hines (University of Toronto) whereby magnetospheric convective motions, which are intensified during magnetic storms, change the vorticity of the lower atmosphere at or near auroral latitudes by viscous coupling. Dessler concluded that there seems to be enough power within the magnetosphere to cause such changes in vorticity, if the power can be directed and coupled effectively.

Another mechanism discussed by Dessler is heating accomplished by direct particle bombardment in the auroral zone. An outstanding intense auroral beam has an energy flux less than 10^{-3} that of sunlight. The heat capacity of the upper atmosphere is so small that the effect of absorbing this energy flux is profound. But the upper atmosphere is thermally isolated from the lower atmosphere by two temperature minima—at the tropopause (15 km) and at the mesopause (80 km). Energy may be converted to forms that can penetrate through these temperature minima to the troposphere, such as infrared radiation and infrasonic waves. But with a power input of only 10^{-3} that of sunlight, Dessler believes it is hard to imagine that the small fraction of this energy that would go into either component would provide a sensible perturbation to the tropospheric system. Roberts believes that a promising trigger mechanism involves the modification of the atmospheric radiation budget

through the sudden formation of cirrus clouds at the tropopause following solar activity.

R. C. J. Somerville reported on numerical experiments on short-term meteorological effects of solar variability performed at the NASA Goddard Institute for Space Studies directed by R. Jastrow. The GISS group carried out a set of numerical experiments to test the short-range sensitivity of a large atmospheric general circulation model to changes in solar constant and ozone amount. On the basis of the results of 12-d integrations with very large variations in these parameters, it was concluded that realistic variations would produce insignificant meteorological effects. The GISS study also concluded that any causal relationships between solar variability and weather, for time scales of 2 weeks or less, will have to rely on changes in parameters other than solar constant or ozone amounts, or upon mechanisms not yet incorporated in the model.

W. W. Kellogg (National Center for Atmospheric Research, Boulder) discussed needed measurements and observations including:

- Continuous monitoring of the energy and pitch angle distribution of geomagnetically trapped electrons and protons in order to determine when they are precipitated into the lower ionosphere.
- Monitoring from balloons in the region of the tropopause the incidence of ionising radiation and any accompanying changes of temperature, conductivity, ozone amount or ultraviolet flux.
- Continuous monitoring from a satellite of absolute solar flux in the near ultraviolet, between 2,000 and 3,000 Å.
- Monitoring global ozone distribution in the region above 30 km.
- Observations of wind systems in the mesosphere and lower thermosphere.
- Detection of high latitude cirrus cloud formation through optical techniques or through the effect of a cirrus deck on the upward infrared radiation in the atmospheric window.
- Satellite optical and radio monitoring of global thunderstorm activity.

In his symposium summary S. I. Rasool (NASA) cautioned against the current practice of correlating solar variations with localised, isolated weather effects instead of global responses. He stressed the importance of the stratosphere as a buffer for solar-meteorological responses and commented that due to its tremendous inertia the relaxation time of the troposphere is so large that short-term tropospheric responses to solar variations cannot be easily identified.

MISCELLANY

Christmas Prize Quiz

Answers to the following questions are all to be found in the pages of *Nature* this year. A prize of a year's subscription to *Nature* is offered for the first correct set of answers opened by the Editor after January 31, or for the best entry.

1. At the start of the year, the Science Research Council became committed to spending £3 million a year on a European venture. What is the venture and who are Britain's partners in it?

2. David's departure caused a New Year surprise. Where did he depart from?

3. From the opposite end of the political spectrum, an arrival in London also seemed surprising in the light of previous refusals. But the pleasure of the scientist concerned was short lived. Who was he and what happened to him in August?

4. After recent moves in musical chairs of astronomy, who is now the Director of the Institute of Astronomy in Cambridge? Who was his predecessor and where is he now?

5. Horns, cols and a hanging valley found by a mariner surprised astronomers. What does their presence indicate?

6. The Council for Scientific Policy died and was reborn in 1973. What is the new name of the Phoenix and who has been chairman of it?

7. Where do we receive communication of the form CCCDDCCCDR?

8. Which countries joined the post-Apollo programme at the last minute?

9. Dr Dixie Lee Ray struck a blow for women's liberation in 1973. How?

10. In the autumn a minister apologised for misleading the House. Who was he and what was the subject under discussion?

11. Who said "we shall be spending thousands of pounds educating young people in social sciences and I cannot imagine any more foolish waste of money"?

12. When is a panda not a raccoon?

13. Which Nobel Prizewinner accused President Nixon of lunatic behaviour? In what context?

14. Nina is approaching retirement. How old will she be when she goes?

15. Who is the latest head of Britain's nuclear power industry?

16. *S. muticum* was found attached to a sheltered shore in Hampshire. Where did it originate?

17. Thorarinnsson, Steinthórsson, Einarsson, Kristmannsdóttir and Oskarsson reported on what violent activity?

18. Laithwaite, Ford and Elliot had

their spring hopes dashed. How?

19. William D. Ruckelshaus granted a temporary reprieve in April. Who to?

20. OH471 extended our knowledge of the Universe. How far?

21. It was suggested in January that there may be 35 million plastic bottles floating in the Pacific. How many red rubber sandals correspond to this?

22. Which Soviet scientist was elected to the National Academy of Sciences in May?

23. A pattern of climatic change affecting the whole Northern Hemisphere was pointed out this year. If the pattern is more than a coincidence, when will the Sahara stop moving south?

24. In 1973 there was a change of editorship of *Nature*. This has happened only four times in 104 years. How many Editors have there been and how many are still living?

25. The power of Flowers gave way to that of another in 1973. Who?

What's in a Name?

AMONG the many botanists in the British Isles are A. M. M. Berrie (Glasgow), K. D. Gardiner (horticulturist, Dublin), B. E. Juniper (Oxford), R. P. Moss (Birmingham), B. L. Moss (Newcastle upon Tyne) and F. Rose (King's College, London).

Fish biologists and oceanographers have in their ranks J. C. Chubb (Liverpool), H. Fish (Essex River Authority), G. R. Fish (Fish Research Division, Rotorua), G. C. Trout (Fisheries Laboratory, Lowestoft) and P. J. Herring (Institute of Oceanographic Sciences).

Zoologists include M. W. Fox (Washington, author of *Behaviour of Wolves, Dogs and Related Canids*), ethologists and collaborators, Robin Fox and Lionel Tiger. It has also been brought to our notice that two zoologists from Birmingham, Drs Cock and Cohen, once collaborated on a paper on the combs of hens.

Miscellaneous: G. C. Cheeseman (National Institute for Research in Dairying, Reading), J. W. G. Musty (Inspectorate of Ancient Monuments, DOE), P. M. Chalk (soil scientist and expert on limestones, Wisconsin), D. L.

26. What do birds come from?

27. Where were a Jumbo number of members faced with a 100% increase in fees?

28. What do baboons use for "napkins"?

29. France's governmental loss was America's academic gain. Who left what to go where?

30. What new society did Paul Sieghart found?

31. What are thrusting everywhere?

32. Skylab followed Apollo. How has Heseltine helped with Skylab's heir?

33. CREST and SPIT; who, what or where?

34. What is IUPAP and how did it fail to meet Professor A. V. Voronel?

35. The Think Tank leaked in September. Where did the leak occur?

36. How old *Homo*?

37. How did *Dimetrodon grandis* keep his cool?

38. A matrimonial binary system did not, after all, make the transition from California to Britain successfully. What was the result?

39. Jesus gained a new master. Who?

40. BASS was conceived by BA. When is the birth?

Entries to: QUIZ, *Nature*, 4 Little Essex Street, London WC2R 3LF.

Coffin (expert on air pollution and environmental health). R. S. Pore (microbiologist, West Virginia), R. T. Severn (civil engineer and consultant for the Severn Barrage, Bristol), E. H. Shove (engineer, City University) and T. E. Gambling (Department of Accounting, Birmingham).

No comment: Z. Ovary (contributor to a conference on obstetrics and gynaecology), Miss Mercedes B. Concepcion (Philippines representative at the Second Asian Population Conference) and Chuck Despina (producer of the BBC TV Horizon programme on acupuncture).

We beg the forgiveness of those readers who feel that their names should have been included but are not; to those who feel that their names should not have been included but are, we offer the reminder that the chief compiler of this information over the past few years has been Sarah Bunney, our News and Views Editor, whose own name has more than one connection with the title of this journal. The fact has not, it seems, escaped the attention of certain telephone callers.

Solution to the BA Cartoon

We asked for identification of the people depicted on the front cover of *Nature*, August 17, 1973. The prize-winning solution given here came from D. P. L. Green, Department of Biophysics, University College, London.

My solution is, proceeding in a clockwise direction from bottom centre: (1) Sir Roderick Impey Murchison (1792–1871); (2) Charles Babbage (1792–1871); (3) Thomas Henry Huxley (1825–95); (4) Dr Richard Owen (1804–92); (5) John Tyndall (1820–93); (6) Sir John Frederick William Herschel (1792–1871); (7) Sir Charles Lyell (1797–1875); (8) George Julius Poulett Scrope (1797–1876).

The ready identity of three of the eight figures immediately raises several interesting questions.

(1) Do the characters depicted bear some close relationship to the structure of the British Association (BA) in 1865?

(2) What relationship do the characters bear to their immediate surroundings?

(3) How much did the artist know and understand of the immediate scientific background of each character?

(4) To what extent do the characters bear a resemblance to other known portraits?

In the Report of the BA for 1865, Sir Roderick Murchison is listed as one of the three trustees as well as the President of Section C, Geology, and Vice-President of Section E, Geography and Ethnology. Dr Richard Owen, as he then was, is listed as an ex-officio member of council, having been President of the BA for the meeting at Leeds in 1858. T. H. Huxley is listed only as a member of the BA. This indicates that we need not be looking for a well defined relationship between the figures and the structure of the BA in that year.

It seems probable that the average reader of *Punch* would not know the appearance of many distinguished men of science of the day. It seems equally probable that the cartoon would lose much of its interest if the reader failed to recognise readily the men depicted.

I turn now to the second and third questions. It is necessary to recount briefly a few biographical details of both Owen and Huxley immediately prior to 1865. Owen was well known in London for having delivered a course of public lectures for 1859, 1860 and 1861 at the Museum of Practical Geology in Jermyn Street. His subject was the fossil remains of animals. His views

were summarised in the Rede lecture delivered at Cambridge in 1859 under the title of "Classification of Mammalia". In April 1860 he wrote an attack on Darwin's *Origin of Species* for the *Edinburgh Review* and Darwin believed him to have inspired the Bishop of Oxford's hostile notice of the same book in the *Quarterly Review*. As for T. H. Huxley, the greater part of his published work for 1855–59 was on fossil forms. The most important problem which then presented itself, both in contemporaneous and fossil form, was the composition of the skull. The doctrine prevalent in England at the time was that which Owen had learned from Goethe and Oken. This method of description obscured the actual anatomical relations of the parts described. Huxley, in his Croonian lecture of 1858 entitled "On the Theory of the Vertebrate Skull", gave a statement of cranial structure which differed from that of Owen, but which Owen failed conspicuously to refute. It is this controversy, rather than their differences over the *Origin of Species*, which I take the audience of curious animals to refer to. Most conspicuous, of course, are their skull-like heads. It is probable that both controversies explain their polite wrestling.

This shows in some detail that the characters do bear some relationship to their immediate surroundings, and this is intuitively obvious, I think, from the general nature of the cartoon. It also shows that the cartoonist had some knowledge of the scientific background of each character.

It now remains to attempt a brief answer to the fourth question, and I will start with Sir Roderick Murchison. In *The History of the Geological Society of London* (London, 1907) by H. B. Woodward there is a reproduction of a painting by Pickersgill of Murchison. From this, it can be seen that the cartoon is not a good likeness. A better likeness exists between the cartoon and the reproduction of an old engraving of Murchison in *The First Hundred Years of the Geological Survey of Great Britain* (HMSO, 1937) by Sir J. Smith Flett. Similarly, a comparison of the depiction of Huxley by the cartoonist with the many extant pictures of Huxley

from this period again serves to underline that we can only expect rather poor likenesses of the figures involved. There is one other problem which should, perhaps, be mentioned at this stage because it is of some importance later. It is not clear how the cartoonist derived his knowledge of the appearance of the figures. This is particularly important if it were to be derived from engravings, because these naturally have the image reversed. This leads to a key feature of identification, the parting of the hair, to be subject to some doubt.

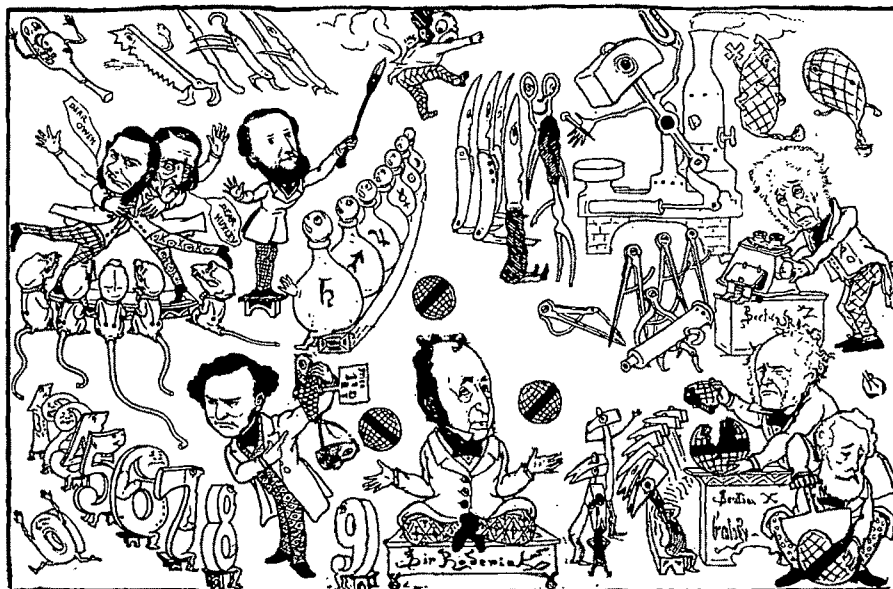
I shall now discuss each separately.

Sir Charles Lyell

The two figures at bottom right are clearly geologists. The most distinguished geologist of his age was undoubtedly Sir Charles Lyell. A photograph in the possession of the Geological Society, which is reproduced in the history of the society mentioned above, places this beyond doubt. Note the pronounced jaw which he possessed, and which comes out fairly clearly in the cartoon.

George Julius Poulett Scrope

Scrope is an exact contemporary of Lyell. In 1828, Scrope published *Considerations on Volcanos* and this enunciated emphatically the doctrine subsequently developed by Lyell and called by him Uniformitarianism. To this extent he was a forerunner of Lyell and their views were generally very similar. He sat as the Member for Stroud from 1833–68, and although he spoke seldom, if at all, he conducted a vigorous campaign of pamphleteering on most social issues of the day, upon which he held what were then considered to be advanced views. As a result, his work as a geologist had slackened considerably. Nevertheless, Scrope and Lyell were considered by their contemporaries as joint protagonists, and the cartoonist's depiction of the two figures together is evidence of the association. (The only other pair is that of Huxley and Owen, and, as already mentioned, they were also associated in the public mind together, although for different reasons.) Finally, there is a photograph of Scrope in the possession of the Geological Society which is reproduced in



The *Punch* cartoon reproduced on the cover of the August 17 issue of *Nature*. It was first published in September 1865. (Reproduced by permission of *Punch*.)

the history mentioned above and which bears a good likeness. The only serious alternative candidate, on the criterion of appearance, is Sir Andrew Crombie Ramsay (1814–91), President of the Geological Society from 1862–64. The objections to this identification rest on the fact that, despite his age in 1865, he was only beginning to rise to public notice and he was not at all associated, in the same manner as Scrope, with Lyell's earlier career.

Sir John Frederick William Herschel

I present the evidence for this ascription in a different order from that for the two above. There exists a photograph of Herschel, taken in 1867, when he was seventy-five. This is reproduced in *The English Face* (London, 1957) by David Piper. Anyone who has seen this picture will find it very difficult to believe that the figure can be anyone else. Nevertheless, there are some problems caused by the surroundings. In 1865 Herschel had been in the forefront of scientific life for fifty years. In 1830 he stood as the 'scientific' candidate for the Presidency of the Royal Society against the Duke of Sussex, and was narrowly defeated. In 1839 he refused a proposal to succeed the Duke. He wrote on a wide variety of subjects. In a paper "On the Chemical Action of the Rays of the Solar System on Preparations of Silver and other Substances" he first described the use of sodium hyposulphite as a fixing agent and used the terms positive and negative in their photographic senses also for the first time. Earlier, he had improved the objectives of microscopes in addition to other important work in optics. He

was always interested in technological improvements, and was one of the jury for scientific instruments at the Great Exhibition. From 1850–1855 he was Master of the Mint and in 1865 he was a member of the committee of the BA which organised the use of balloons for meteorological and physical observations.

This outline constitutes only a small part of his activities but it does serve to explain most of the surroundings in the cartoon. The peculiar device which the figure is holding is less clear. It may be a reference to his photographic work or to his work on microscopes. In either case, the legs of a small man sticking out are, to me, obscure. As for the steam hammer, this again presents difficulties. It could, of course, refer to some process used either at the Mint or in the manufacture of instruments. There is another explanation. One other possible candidate for the figure is the inventor of the steam hammer, James Nasmyth (1808–90). Nasmyth was himself an instrument maker and keen astronomer, and he knew Herschel well. On Herschel's death, Nasmyth put him "supremely at the head" of all the scientific men of his acquaintance. Consideration of Nasmyth as the figure depicted is not itself without objections, however. There is no connection to my knowledge between him and balloons and I do not think that he was as conspicuous a public figure as Herschel. He was also much younger, yet the figure under discussion is the oldest in appearance in the cartoon. Finally, although Nasmyth was melancholic in appearance, rather as Herschel, he also possessed a pronounced curl of hair in the centre of his forehead.

John Tyndall

The surroundings of this figure include the series of bottles with signs upon them. These signs are Berzelius's notation for certain metallic elements and are derived from the astrological notation for certain members of the Solar System. It marks this figure out as a physical scientist. The hot poker in the left hand, I take it, indicates a connection with heat.

In 1853, Tyndall became Professor of Natural Philosophy at the Royal Institution where he was Faraday's closest colleague until the latter's death, whereupon Tyndall succeeded him as Director. His early researches were on magnetism, but by 1865 he had for many years been interested in heat. His book *Heat Considered as a Mode of Motion* was published in 1863. It was widely read. It is difficult not to think that the character jumping in response to the hot iron is not a visual pun on heat as a mode of motion. There is one problem with this ascription, the parting of the hair. Tyndall parted his hair on the left. In mitigation may be stated two facts. First, his hairline receded markedly on each side of his head and this may be loosely represented by the cartoonist as a parting. Second, there existed in about 1860 an engraving by H. Adlard of Tyndall, with Faraday, in which, of course, the parting is reversed. This problem has been discussed in the preamble. (I would just add that a cartoon of T. H. Huxley, reproduced in *T. H. Huxley* (London, 1959) by Cyril Bibby shows Huxley with his parting on the wrong side.) The overall likeness of the cartoon to Tyndall is tolerable, especially in respect of the beard.

Charles Babbage

This is again not without difficulties in ascription. The three salient features of the cartoon are the numbers, the fish and the price tag. The numbers I take to refer either to an arithmetician or to somebody whose interest lay in computation. The figure who immediately springs to mind in both cases is Charles Babbage. He wrote widely. His *Reflections on the Decline of Science in England and Some of its Causes*, published in 1830, was an attack on the management of the Royal Society which contributed materially to the founding of the BA in 1831 at York. In 1832 we have the *Economy of Machines and Manufactures*; in 1848, the *Thoughts on the Principles of Taxation, with reference to a Property Tax and its Exceptions*, and in 1851, *The Exposition of 1851; or, Views of the Industry, the Science, and the Government of England*. In addition he wrote papers on a great range of subjects, but he is, of course, best remembered nowadays for his work on calculating

machines. In the introduction to the second edition of *The Exposition of 1851* Babbage added, "On one or two points I differed entirely from the opinion of those to whom its management was confided. The questions of *the site of the building* and of *affixing prices to articles exhibited* were the most important."

Chapter VIII is wholly devoted to prices and a description of how Babbage saw a free market operating. On page 93 we have, as one of several examples, the following:

"Different prices for the same article are often demanded by retail tradesmen according to the supposed position of the purchaser. Fish, for example, which varies much in price and is at times very cheap will seldom be found charged to the household bill much below the average price. . . ." Babbage was widely known to the public for his forthright views, and although this was written fourteen years before 1865, it is just the sort of thing which would become stuck in the public's mind.

If it is Babbage, the figure was the same age as Murchison and Herschel and yet, of the three, is clearly the youngest. In a photograph of Babbage, reproduced in *Irascible Genius; A Life of Charles Babbage* (London, 1964) by Mabothe Moseley, he looks younger than he was. This picture also shows the texture of his hair and the marked indentation at the parting shown in the cartoon. Finally, the figure in the cartoon looks somewhat impatient and irascible.

Let me be the first to state that I am not wholly convinced of my own solutions. It is in the nature of the problem that I could not arrive satisfactorily at the solution merely by elimination of alternative candidates because of the general paucity of my knowledge. Rather, I have tried to make sensible guesses and justify them to the best of my means.

Note

We also said that a mention of the Stodare trick appeared beneath the cartoon. For good measure Dr Green appends the following information:

The Stodare trick mentioned in the caption is one of two named after Colonel Stodare, the stage name of John English (1831-66). In the *Encyclopaedia Britannica* for 1910 there is a reference to a trick as follows:

"The sword and basket trick was common in India many years ago. In one form it consisted in inverting an empty basket over a child upon the ground. After the child had secreted himself between the basket bottom and a belt concealed by a curtain painted to look like the actual wicker bottom, a sword was thrust through both sides of the basket, the child screaming and squeezing upon the sword a blood-coloured liquid from a sponge. When the performer upset the basket the child could not be seen; but another child, similarly costumed, suddenly appeared among the spectators, having been supported by a pair of stirrups under the cloak of a confederate among the bystanders."

Chess Problems

THE most familiar form of chess to most people is the serious and competitive game, the world of match play, tournaments and grand masters. There exists, however, a different form of chess, the quieter branch of problems and studies where the chief aim is generally that of amusement only.

One type of chess problem is to present a situation which appears on the surface to be quite easy to solve but which in practice does not turn out to be so simple. For example, a problem requiring a 'mate in one' probably gives the impression of being insultingly simple, yet examples of this type of problem do exist where the solution is not immediately obvious. Problems 1 and 2 below are both mates in one and may not delay most solvers long from their Christmas turkeys, but it is important to be quite sure that the sole correct solution has been found for each problem.

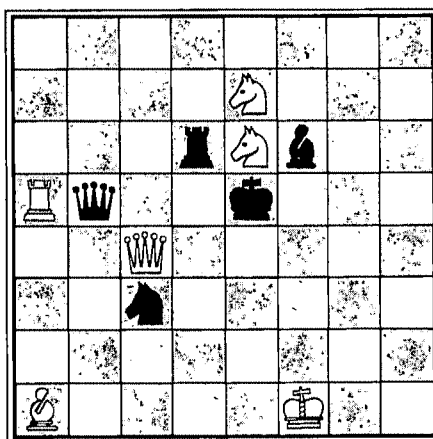
Problem 3 is based on an idea demonstrated by Sam Loyd over a hundred years ago. It is a mate in two, which may give certain alternating impressions during the course of solving it:

first, 'impossible'; second, 'trivial'; third, 'impossible' once again, before the real point of the problem is spotted.

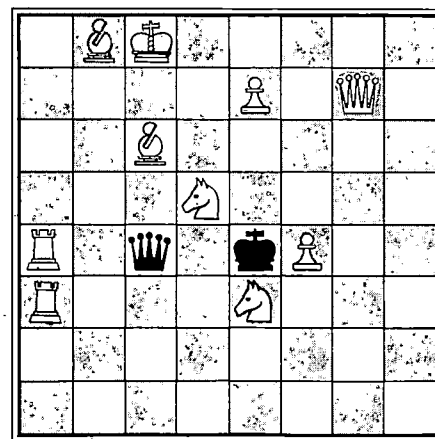
There is a tradition amongst problemists that a problem position must be a 'legal' one. In other words, it must be a position that could, theoretically, be reached from the starting position of a game of chess (unless it is specifically stated to be a "fairy chess" problem). This has given rise to some puzzles where moves have to be worked out in a retrograde fashion in order to determine that only a single sequence of moves could have been 'legally' played immediately leading up to the position in hand. Problem 4 is an adaptation of an old idea showing that only one 'legal' move is possible as White's immediately preceding move to the position in the diagram. But a modicum of retrograde analysis is necessary to demonstrate that the solution is a unique one, and it is worth noting that the line-up of Black pawns on the queen's rook file is a relevant feature of the problem.

J. P.

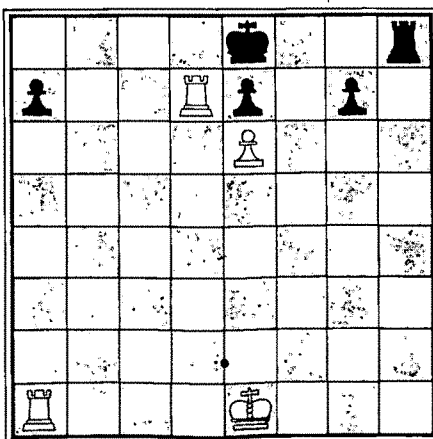
(Solutions will be found on page 438 of this issue.)



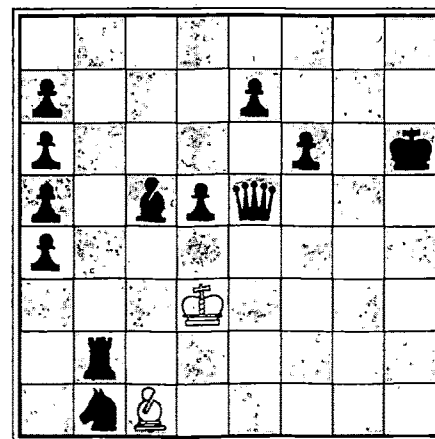
1 White mates in one move.



2 White mates in one move.



3 White mates in two moves.



4 What must White's last move have been?

Molecular Evolution of Myoglobin and the Fossil Record: a Phylogenetic Synthesis

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An ancestral myoglobin chain has been deduced by comparing the differences in the amino acid sequences of eighteen living species and assessing from the fossil evidence the probable times of divergence of their ancestors.

THE molecular evolution of myoglobin can be investigated by comparing the differences in the eighteen species for which its amino acid structure is known¹⁻¹⁷ (see Fig. 1 for the complete sequence of human myoglobin), and probable times of divergence of the ancestors of these species can be assessed from fossil evidence. The biochemical and palaeontological information has been integrated in a cladogram and a possible ancestral myoglobin chain deduced. The reconstructed pathways of mutation support most of the assumed phylogeny but also suggest possible modifications, and provide information about rates of molecular evolution.

The number of amino acid differences between species is shown in Fig. 2. Although similarities may result from close relationship, or convergence, or possibly transduction^{18,19}, we have not taken the latter into account.

The evolutionary study of myoglobin cannot be divorced from its function. Myoglobin resembles haemoglobin at the haem contacts, but not at those sites peculiar to haemoglobin which are responsible for haem-haem interaction^{8,20}. The internal hydrophobic residues are similar in all globins. Among the eighteen mammalian myoglobins mutations have been fixed at only sixty-seven sites out of 153. These involve sixty out of 120 surface residues (including three of ten external haem contacts) and only seven out of thirty-three internal sites (including two of twelve haem contacts). At all three external haem contact sites which have accepted a change, the residue is constant in seventeen out of eighteen species.

	MAN	CHIMPANZEE	GORILLA	BABOON	MACAQUE	WOOLLY MONK	SQUIRREL MONK	MARMOSSET	GALAGO	SPOTT. LEMUR	HARBOR SEAL	PORPOISE	DOLPHIN	SPERM WHALE	HORSE	OX	SHEEP	KANGAROO	LAMPREY	GLYCERA
1	1	6	7	16	17	14	23	22	24	20	28	26	19	29	25	22	105	102	MAN	
2		1	6	17	18	15	24	21	23	19	25	24	18	28	24	23	105	102	CHIMPANZEE	
5			1	6	15	16	13	24	23	25	21	27	26	20	30	26	23	105	GIBBON	
1				1	13	12	11	22	21	23	22	27	26	18	29	25	22	106	BABOON	
12					1	12	10	21	21	23	22	27	26	18	29	25	22	106	MACAQUE	
4						4	4	19	25	26	31	29	19	29	25	22	107	105	WOOLLY MONK	
4							4	23	27	28	32	31	19	30	26	23	107	106	SQUIRREL MONK	
23								17	23	24	29	27	17	28	24	23	106	105	MARMOSSET	
21									21	28	26	30	27	22	30	27	30	102	GALAGO	
17										17	18	23	24	12	23	20	24	102	SPOTT. LEMUR	
17											17	23	26	20	28	27	27	104	HARBOR SEAL	
12												12	15	16	23	29	105	103	PORPOISE	
9													9	21	29	28	32	104	DOLPHIN	
19														19	30	27	31	103	SPERM WHALE	
18															18	26	25	105	HORSE	
6																6	35	102	OX	
31																	31	103	SHEEP	
103																		103	KANGAROO	
97																			97	LAMPREY
																				GLYCERA

Fig. 2 Matrix showing the number of amino acid differences between the myoglobins of eighteen mammals and the haemoglobins of lamprey and *Glycera*.

Of the numerous differences between haemoglobin and myoglobin, four deserve comment. (1) There are thirteen residues participating in salt bridges which help to maintain the shape of the monomer^{21,22}. With one exception (E5 Lys) these residues differ between the globin families, but amongst myoglobins only five of the thirteen have accepted mutations, and these are highly conservative (Asp $\leftrightarrow$ Glu, Lys $\leftrightarrow$ Arg), except for kangaroo (G3 Gln instead of Lys). (2) In the myoglobins G5 Leu is invariant, and in the haemoglobins (except *Chironomus*) G5 is Phe (ref. 23), which helps to maintain the haem plate in the more upright position in deoxyhaemoglobin²⁴. An abnormal human haemoglobin "Heathrow" also has Leu at β G5 (ref. 25). This variant has a very high oxygen affinity, and it is probable that G5 Leu has a part in conferring that characteristic on myoglobin. (Myoglobin, being a monomer, would be expected to have a high oxygen affinity like a single haemoglobin chain. (3) H23 Tyr is helical in myoglobin but

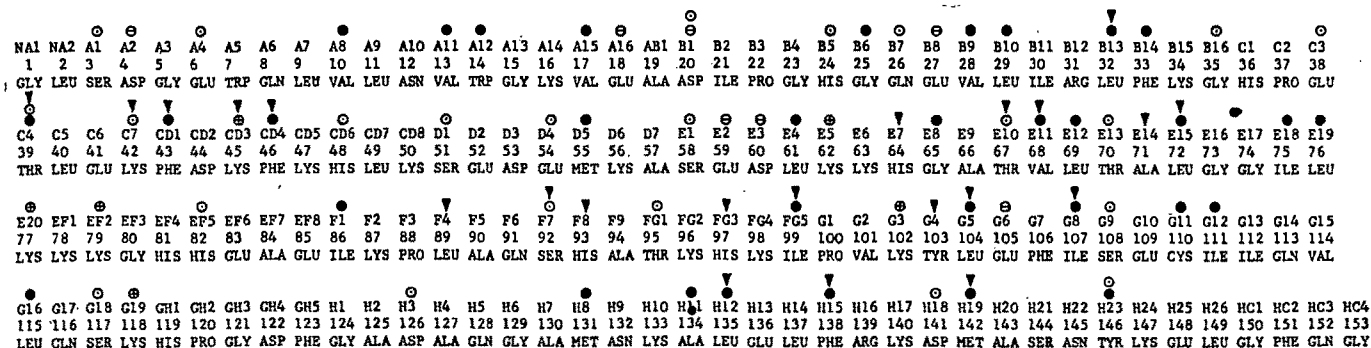


Fig. 1 Complete sequence of human myoglobin (with helical and sequential numbers). ▼, Haem contacts; ●, internal residues; ⊕, ⊖, charged residues forming salt bridges; ○, residues involved in hydrogen bonding.

non-helical (HC2) in haemoglobin²⁶ where this invariant Tyr participates in the transition from the deoxy- to oxy-conformation of the tetramer²⁷. In the monomeric myoglobin the hydrogen bond which this residue forms with the main chain at FG5 (refs 28 and 29) must be of singular structural importance. (4) In the myoglobins the C helix and the CD interhelical bend form an external flat plane where the charged residues C3, C6, CD2, CD5 and CD8 are invariant. The invariant FG4 also falls into this plane. Preservation of this region may be due to interaction with other molecules or mitochondria during the facilitation of oxygen diffusion^{30,31}. In haemoglobin, C3, C6 and FG4 are tetrameric contacts²⁹, and the strict preservation of a difference in this part of the myoglobin surface may guarantee its monomeric character.

Haemoglobins and myoglobins have a common ancestral polypeptide chain and so two distant haemoglobin chains have been compared with those of mammalian myoglobins (Fig. 2). One was the major monomeric component of haemoglobin from the marine worm *Glycera*³² and the other was haemoglobin V from the lamprey *Petromyzon*³³. These forms have evolved separately from the ancestral stock leading to mammals for not less than 540 and 420 m.y. respectively. In both cases 136 sites were comparable, insertions and deletions having been eliminated. In comparing *Glycera* with lamprey twenty-seven of 124 homologous sites were identical.

The similarity in the number of amino acid differences between these haemoglobins and the myoglobins is remarkable (Fig. 2). In each case they average 104.5 ± 2.5 residues, in spite of the fact that the mammalian myoglobins average twenty-five differences between them. But the apparent constant rate of molecular evolution when *Glycera* and lamprey globins are compared with those of mammals reflects amino acid differences without taking into account that during a minimum of 400–500 m.y. of divergence even the minimum mutation distance is inaccurate^{34,35}, because undetected mutations can lead to errors greater than 100%.

When two globin chains are compared ignoring insertions and deletions, then irrespective of their relative divergence (even considering plant haemoglobin)²³, a minimum proportion of approximately 16% of their residues is the same. Except for the invariant F8 His and CD1 Phe the location of these differs from pair to pair. There is a limit to the number of amino acid differences that a given molecule can accept and it can be argued that the variable sites are interdependent because a new side chain will affect its neighbours in the tertiary structure, and so put some constraint on the residues involved in the folding of the molecule. A similar observation has been made for cytochrome *c* (ref. 36). Setting aside convergence and transduction it appears that the characteristic tertiary structure of the globin family has been maintained within a small degree of variation during at least 540 m.y. of evolution³⁷.

Phylogenetic Chart

It is now essential to explain the basis of our phylogenetic chart (Fig. 3). The "Geological Society Phanerozoic time-scale (1964)"³⁸ has been used with modifications suggested in the Supplement³⁹. Necessary qualifications regarding Tertiary dates, especially for the Miocene, are fully discussed by Berggren⁴⁰. The pattern of branching largely reflects the grouping of the species in systematic classification but gives no indication of rank in systematic hierarchy. To determine the positions of branching we asked the question: at what point in time can it be shown that the ancestors of these two living forms had diverged? We rejected speculations regarding earlier dichotomies which require assumptions about fossils not yet found, and in consequence many of our points are likely to be later than the actual event.

Trichotomies do not represent our opinion of the phylogenetic pattern but reflect a failure in the time resolution of the available fossil evidence and result from the superimposition of two adjacent dichotomies; their order of occurrence can be suggested on the basis of comparative anatomy. Each point will be discussed using the reference numbers on Fig. 3.

(1) Polychaetes are too specialised to have been ancestral to chordates and *vice versa*, and so the earliest known representative of either group provides evidence that they had diverged. *Spriggina* and *Dickinsonia* (Precambrian/Cambrian transition, Australia)⁴¹ are recognised as possible polychaetes. *Pikaia*, *Miskioia*, *Canadia* and *Worthenella* (Middle Cambrian, British Columbia) are generally accepted as polychaetes⁴²; although none is undoubted this group probably includes the earliest known polychaete. *Palaeoscolex* (Tremadocian, England) was not originally described

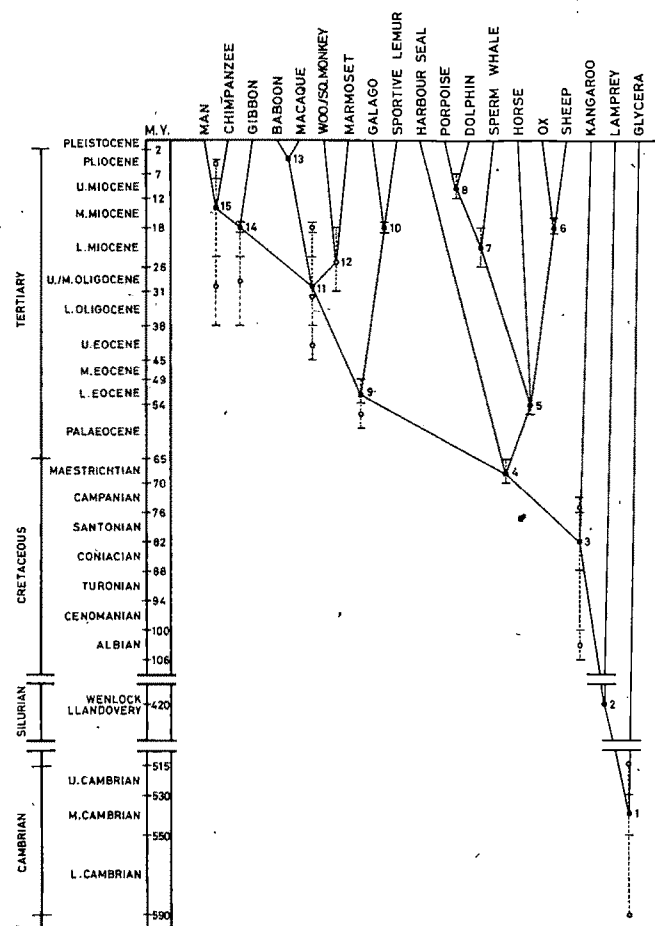


Fig. 3 Phylogenetic chart of the species included in this study, the points of divergence being based on the fossil record and numbered for reference purposes. The most probable point is indicated by a solid circle (●), possible alternatives by open circles (○). Horizontal lines indicate the time range within which a fossil cannot be definitely fixed; where the centre point of this range was used fractions were rounded to the nearest million years older. Some radiometric dates have been placed on the absolute time scale regardless of stratigraphical correlations. *Homo sapiens*, man^{3,8,10,11}; *Pan troglodytes*, chimpanzee¹¹; *Hyllobates agilis*, gibbon¹⁰; *Papio anubis*, baboon¹²; *Macaca fascicularis*, macaque¹²; *Lagothrix lagotricha*, woolly monkey^{15,16}; *Saimiri sciureus*, squirrel monkey^{15,16}; *Callithrix jacchus*, marmoset^{15,16}; *Galago crassicaudatus*, galago¹⁷; *Lepilemur mustelinus*, sportive lemur¹⁷; *Phoca vitulina*, harbour seal⁴; *Phocaena phocaena*, porpoise⁴; *Delphinus delphis*, dolphin^{6,9}; *Physeter catodon*, sperm whale¹; *Equus caballus*, horse²; *Bos taurus*, ox⁵; *Ovis aries*, sheep^{13,14}; *Macropus giganteus*, kangaroo⁷; *Petromyzon marinus*, lamprey³³; *Glycera dibranchiata*³².

as a polychaete⁴³; it has since been both doubted as an annelid⁴² and regarded as the earliest record of polychaete scolecodonts⁴⁴.

(2) Assuming a monophyletic origin this dichotomy can be equated with the earliest evidence of Gnathostomata, provided by the acanthodian *Nostolepis* (Llandovery/Wenlock, Czechoslovakia)⁴⁵. The extent of stratigraphical uncertainty is not known.

(3) Metatheria and Eutheria diverged from a common therian stem, but it is controversial whether this stem was metatherian or eutherian or neither. The affinities of *Pappotherium* and *Holoclemensia* (Albian, Texas), claimed as eutherian and metatherian respectively⁴⁶, are open to question^{47,48}. *Zalambdalestes* and *Kennalestes* (Bayn Dzak, Mongolia) are undoubted eutherians and unsuitable as ancestors to Metatheria. Kielan-Jaworowska has suggested a possible Coniacian/Santonian age for the Bayn Dzak fauna⁴⁹, as indicated on our chart, but McKenna prefers a Cenomanian age⁵⁰. A record of Santonian marsupials in North America⁵¹ is not currently accepted⁴⁷ but marsupials and placentals coexist in the Lower Campanian (Alberta)⁵², and this is shown as a possible point in case Bayn Dzak turns out to be younger than expected.

(4) This point emerges as a trichotomy. Considering first the separation of Primates from the basic eutherian stock, *Purgatorius* (known by many teeth in Lower Palaeocene, Montana, and one tooth from Maestrichtian, Montana) has been claimed as the earliest known primate^{53,54}. This form is little different from several early eutherians, including arctocyonid *Condylarthra*^{55,56}, and its assignment to the Primates has been doubted⁴⁸. It is generally accepted that the order *Condylarthra* was ancestral to Artiodactyla and Perissodactyla and probably to Cetacea. The earliest known condylarthran is *Protungulatum* (Maestrichtian, Montana)⁵⁷. From this, if we accept *Purgatorius* as a primate and *Protungulatum* as an ungulate, both first known at the same time, then the remaining eutherian stock is likely to include the ancestors of the Carnivora. The earliest Carnivora are the miacids *Proictis* and *Ictidopappus* (Middle Palaeocene, North America), although a possible *Ictidopappus* tooth has been reported from Lower Palaeocene⁵⁸. It is, however, possible that miacids were derived from arctocyonids, in which case the phylogenetic chart would have shown a dichotomy between Primates and *Condylarthra* followed by a dichotomy on the condylarthran line giving rise to the Carnivora, but on the present evidence we prefer to remain uncommitted. If *Purgatorius* should prove not to be a primate, then the trichotomy would become a dichotomy between *Condylarthra* and the remaining eutherian stock, which would lead to a Middle Palaeocene dichotomy between Primates and Carnivora.

(5) This point is represented by a trichotomy. Considering first the dichotomy between Artiodactyla and Perissodactyla, it can be defined by the differentiation of either order from the *Condylarthra*. The perissodactyl *Hyracotherium* (Late Palaeocene/Eocene transition, Wyoming)⁵⁹ just antedates several artiodactyls, including *Diacodexis* in the lowest Eocene^{60,61}.

There is a body of opinion that Cetacea may have arisen from mesonychid condylarthrans^{60,62} and it could be argued that differentiation of mesonychids from arctocyonids represents the point of divergence of Cetacea. On the other hand, it is not inconceivable that Cetacea arose from arctocyonids through another intermediate group still unknown. It is thus assumed that when the Artiodactyla and Perissodactyla had diverged from the *Condylarthra*, the remaining condylarthran stock would have included the ancestors of Cetacea. The earliest recorded cetacean is *Anglocetus* (Lower Eocene, England)⁶³.

(6) We have accepted that *Eotragus* (Burdigalian, Europe)⁶⁴ is likely to be connected with the ancestry of oxen and bovine antelopes but is unlikely to have given rise to either

gazelles or sheep⁶⁵. Probable time limits on a radiometric scale are based on Van Couvering's comparative study of the European Neogene⁶⁶.

(7) Among toothed whales (Odontoceti) the earliest indication of dichotomy between sperm whales (Physeteridae) and the remaining stock (including dolphins and the ancestors of porpoises) is provided by *Physeter* itself (Lower Miocene, Europe) and by *Apenophyseter*, *Diaphorocetus* and *Idiorophus* (Lower Miocene, South America)⁶⁷.

(8) We cannot rule out the possibility that dolphins (Delphinidae) were ancestral to porpoises (Phocaenidae), or *vice versa*, and so their divergence cannot be established until such time as both groups were present. Several dolphins are recorded from the Lower Miocene but the earliest known porpoises are *Palaeophocaena* and *Proto-phocaena* (Upper Miocene, Europe)⁶⁷⁻⁶⁹. If Delphinidae did not give rise to Phocaenidae, then this dichotomy would need to be moved to the point of first appearance of Delphinidae; it would then coincide with the previous dichotomy and form a trichotomy.

(9) Assuming that the suborder Anthroipoidea (which includes monkeys, apes and man) arose from the suborder Prosimii (which includes lemurs) then at first sight this dichotomy can be fixed at the earliest record of Anthroipoidea. On the other hand, within the Prosimii it is generally accepted that Anthroipoidea arose from the infraorder Tarsiiformes. As it is most unlikely that Tarsiiformes gave rise either to the infraorder Lemuriformes or to the infraorder Lorisiformes, (which includes *Galago*) then the dichotomy can be represented best by the earliest known member of the Tarsiiformes (excluding the Paromomyidae, which some authorities now place in the infraorder Plesiadapiformes)⁵⁶. *Berruvius* (Upper Palaeocene, France) and *Navajovius* (Upper Palaeocene, Colorado) are possible candidates, but Szalay regards both as paromomyids⁷⁰. We have indicated Lower Eocene as the most probable point by which time several anaptomorphid tarsioids (including *Tetonius*) were present⁵⁶.

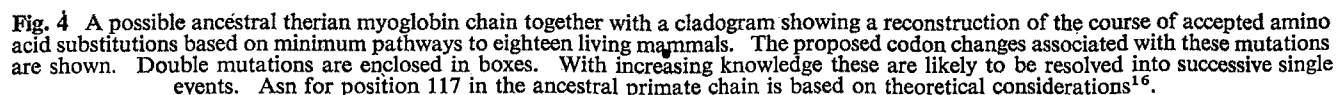
(10) There is general agreement that the Lorisiformes were derived from early members of the Lemuriformes and their divergence cannot be established until such time as both groups were present. Lemuriformes are represented in the Eocene, but Lorisiformes are unknown before *Progalago* and *Komba* (Miocene, Rusinga and Songhor, Kenya)⁷¹, for which radiometric dates are available^{72,73}.

(11) The divergence between the Ceboidea (New World monkeys), the Cercopithecoidea (Old World monkeys) and the Hominoidea (including apes and man) emerges as a trichotomy. The earliest possible point represents the suggestion that *Amphipithecus* and *Pondaungia* (Upper Eocene, Burma) could be catarrhines, perhaps Hominoidea⁵⁶. A second possible point represents the single mandible of *Oligopithecus* (Yale quarry E, Fayum, Egypt) which is probably catarrhine and has been interpreted as a hominoid⁷⁴. The most probable point represents an estimated age for the hominoid *Propliopithecus* and the parapithecine cercopithecoid *Apidium* (Yale quarry G, Fayum)⁵⁶.

The remaining tarsioid-anthropoid stock, which was neither hominoid nor cercopithecoid, presumably included the ancestors of the Ceboidea, but with the exception of the possible ceboid *Branisella* (Lower Oligocene, Bolivia)⁷⁵, none is known before *Dolichocebus* and *Homunculus* (Upper Oligocene/Lower Miocene, Patagonia)⁷⁶.

It is not universally accepted that *Apidium* and *Parapithecus* are cercopithecoid, and so we indicate a radiometric date for the monkey *Victoriapithecus* (Miocene, Rusinga)⁷⁷ as a later possible point. The cercopithecoid *Prohylobates* (Miocene, Egypt) represents an alternative to this point but its age is uncertain⁷⁴.

(12) Within the Ceboidea this dichotomy represents the divergence between Callitrichidae and Cebidae. Their relationship is obscure and the possible point is based on



European Monographs in Social Psychology Number 5**Health and Illness****A Social Psychological Analysis****Claudine Herzlich translated by Douglas Graham****December 1973, xiv+160 pp., £3.80/\$10.75**

0.12.344150.1

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Spore Research 1973**Edited by A. N. Barker, G. W. Gould and J. Wolf****January 1974, approx. 330 pp., £5.50/\$15.50**

0.12.078752.0

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0.12.648150.4

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0.12.613332.8

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0.12.428950.9

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the suggestion that *Dolichocebus* is a callitrichid and *Homunculus* a cebid⁷⁸, but Simons regards both as cebids⁵⁶. In Fig. 3 this is the only dichotomy based on a possible point, but in the absence of other fossil callitrichids we cannot indicate a more probable point. Among the Cebidae none of the few known fossils gives any indication of a possible time of divergence between squirrel monkey and woolly monkey.

(13) This dichotomy represents the divergence of baboons from the less specialised stock which includes macaques. *Dolichopithecus*, *Procynocephalus* and *Libypithecus* have been interpreted as terrestrially adapted macaques rather than baboons⁵⁶, and the gelada *Theropithecus* (= *Simopithecus*) is first known at about the same time as *Parapapio*, which appears to be ancestral to the modern baboon *Papio*⁷⁹. The earliest record of *Parapapio* (Kanapoi Beds, Turkana, Kenya) is dated at about 4 m.y. (ref. 80).

(14) Within the Hominoidea this dichotomy represents the divergence between Hylobatidae (including gibbon) and Pongidae (including chimpanzee), but their relationship is obscure. The earliest possible point represents the suggestion⁸¹ that *Aeolopithecus* (Yale quarry I, Fayum) has hylobatid affinities, in contrast to the better known *Aegyptopithecus* (same site) which is accepted as a pongid. Excluding *Limnopithecus legetet*, now doubted as a hylobatid (P. J. Andrews, personal communication), the most probable point is based on '*Limnopithecus*' *macinnesi* and *Dryopithecus* (*Proconsul*) at Rusinga⁸², the former accepted as a hylobatid and the latter as a pongid.

(15) The earliest possible date represents a minority view, advocated most recently by Kurten⁸³, that *Propliopithecus* is an ancestral hominid. A more widely held view is that the Hominidae arose from within the Pongidae at some later stage. The most probable point represents *Ramapithecus*, which is widely accepted as a hominid. It is recorded from both India and Africa and the most accurately dated find is at Fort Ternan, Kenya⁸⁴, with a radiometric age of 14 m.y. (ref. 73). For this most contentious point we have indicated that which is generally accepted among primatologists as most probable, but we have doubts as to whether sufficient is known about *Ramapithecus* to be sure of its hominid affinity. The earliest undoubted hominid is *Australopithecus* (Lothagam 1 Bed, Kenya) with an estimated date of 5 m.y. (ref. 80).

Reconstruction of Possible Ancestral Therian Myoglobin

Figure 4 shows a cladogram (the pattern of branching being based largely on the phylogenetic chart) indicating how the mutations could have taken place along the different lines leading to the eighteen mammal species, together with a reconstruction of a possible ancestral therian myoglobin. Most of these mutations could be allocated with confidence. In a few cases, however, there was more than one possibility and the amino acid decided on was the most economical from the point of view of the genetic code. The uncertainty is less when species are closely related (baboon-macaque) and increases with distance (kangaroo). As the genetic code is degenerate it was possible to limit the number of codons on several occasions when subsequent mutations were taken into account, assuming single point substitutions in the triplets. Published partial sequences for myoglobin were also considered: dog⁸⁵, badger⁸⁶, humpback whale⁸⁷, pig⁸⁸ and chicken⁸⁹, as well as our preliminary results on the hedgehog and *Tupaia*.

The cladogram shows 147 mutations fixed in at least 82 m.y. of evolution; seventy-four of these are parallel changes which have occurred at twenty-four positions. At some of these positions parallel changes occurred several times: sixteen events have occurred at two positions, eleven events

at three positions, one at four and one at five. Seven detectable double mutations were found; they are at positions 57 Arg in the harbour seal, 85 Asn in the porpoise, 122 Gln in the dolphin, 67 Val in the horse, 9 Ala and 142 Ala in the ox and 74 Asn in the kangaroo. The cladogram also shows seven detectable back mutations, 13 Ile in the branches leading to the cebids and *Galago*, 23 Gly in the pongid branch, 112 Ile in the woolly monkey, 113 Gln in the catarrhine branch, 21 Val in the sportive lemur and 152 Gln in the sperm whale.

The trichotomies shown on the phylogenetic chart (Fig. 3) were resolved into successive dichotomies in the cladogram (Fig. 4) because certain amino acids were shared by two instead of three branches: apes and cercopithecoids have in common residues 66 Val, 86 Ile, 110 Ser and 113 Gln; harbour seal and Condylarthra shared residues 66 Asn, 101 Ile and 116 His; and horse and artiodactyls share residues 34 Thr, 109 Asp and 122 Asn; the branch leading to the dolphin has an immediate common ancestor with the sperm whale, instead of with the porpoise. According to traditional zoological opinion the porpoise and dolphin belong together in the Delphinoidea and the sperm whale belongs to the Physeteroidea. It is then striking that the sperm whale and dolphin share residues 1 Val, 12 His, 15 Ala, 28 Ile and 74 Ala. On the other hand, there is only one residue shared by the porpoise and dolphin, 121 Ala. To join the dolphin with the porpoise instead of with the sperm whale branch requires either parallel evolution of the lines leading to sperm whale and dolphin and an independent fixation of five mutations over a period of not less than 22 m.y., or that these five changes happened after the ancestral cetacean branch separated from the Condylarthra. In the latter case the line leading to the porpoise would have had to accommodate five back mutations. Both these possibilities are unlikely even taking into consideration that powerful selection forces are exerted upon the myoglobin of diving mammals⁹⁰. Comparison of other molecules from the three species will help to resolve this problem.

The ox has the largest number of fixed mutations and one wonders whether this is the result of selection by man, combined with the possibility of genetic drift in small populations⁹¹. A similar phenomenon was, however, not found in the sheep. To resolve this problem we propose to study the myoglobin of wild oxen. It is interesting that a large number of fixed mutations has been claimed for calcitonins in the ancestral artiodactyl stock⁹².

In the palaeontological tree the woolly monkey and squirrel monkey were not distinguished because no fossil evidence has been discovered to date their divergence. However, their common ancestry is indicated by the shared residues 13 Ile and 81 Gln and their later divergence by 66 Val, 112 Ile and 114 Ala in the woolly monkey and 66 Thr and 106 Leu in the squirrel monkey.

Figure 5 shows that the lineages of *Galago* and *Lepilemur* (after they diverged from their common ancestor) appear to have two of the highest mutation rates, but the only fossil evidence documenting their separation is dated at 18 m.y. If the two prosimians diverged from their immediate ancestor not long after it separated from the branch leading to the anthropoids, then this would fit well with the separation of Madagascar from the African mainland, which probably isolated the island's prosimians about 40 m.y. ago⁹³.

The total number of mutations fixed in the different lineages during the past 82 m.y. ranges from 13–28 (mean 19.3). All of these totals (with the marginal exception of that for the ox) fall within two standard deviations from the mean. Although this is consistent with the hypothesis of a constant rate of molecular evolution, it must be emphasised that inability to demonstrate a significant difference from the mean does not prove identity. We are, of course, aware that similar values are to be expected for

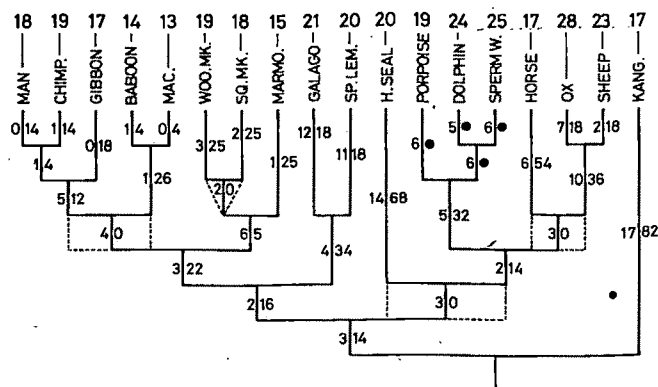


Fig. 5 Cladogram showing on the left of each branch the minimum number of amino acid substitutions, and on the right an estimate of elapsed time based on the most probable points of divergence. The minimum total of accepted mutations is shown for each species since eutherian/metatherian divergence. Double mutations are counted as two steps. As the fossil evidence for the divergence within the Cetacea differed from that used in the cladogram no times (●) are given for this group. The vertical and horizontal broken lines indicate resolved trichotomies.

species which have diverged relatively recently because a large part of their ancestry has followed an identical course. Nevertheless, similar values are obtained for the four groups which diverged more than 68 m.y. ago, the mean value for primates being 17.4, for condylarthran derivatives 22.7, for the harbour seal 20 and for the kangaroo 17.

Although it has been accepted that the rate of evolution of anatomical structures is variable^{94,95} this has been disputed for single molecules⁹⁶⁻¹⁰⁴. Figure 6 shows the relationship between time and the number of fixed mutations along the different branches leading to the living species. We note that periods of apparently low rate of fixed mutations are often followed by apparently high rate episodes, and vice

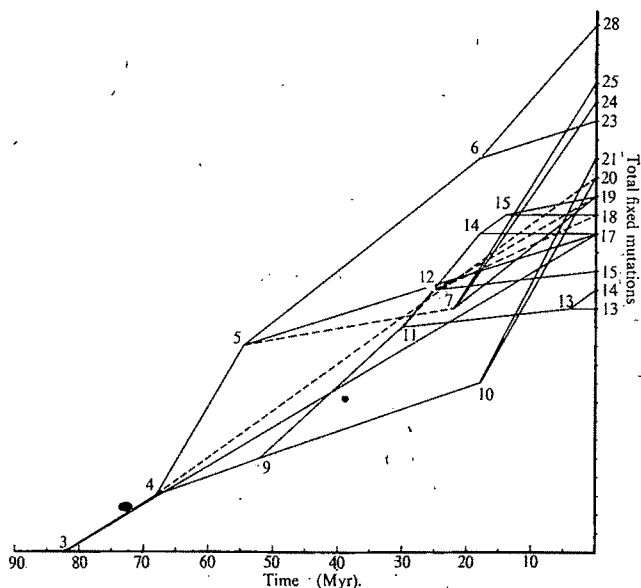


Fig. 6 Relationship between time and the number of fixed mutations along the branches leading to the living species. Numbered points of divergence and pattern of branching as in Fig. 3, except the cetaceans which are shown as a trichotomy because of the different pattern suggested by their myoglobins. The slope of the line reflects the rate at which mutations have been fixed but where trichotomies can be resolved the slope of some lines (broken) is known to be less reliable because the time of divergence differs from the point indicated. Other extreme changes of slope are discussed in the text.

versa; these fluctuations could result in a few cases from the chosen interpretation of the pathway of mutations or they could reflect inaccuracies in the time of divergence, or they could be real. For example, point 10 is probably too late owing to imperfection of the fossil record and points 14 and 15 may be too early owing to problems of interpretation of the fossils.

Differences in the rate of fixation can be demonstrated (Fig. 5) by comparing the number of mutations along two lines rising from the same point, for example, six mutations (horse) compared with twelve (sheep) in 54 m.y. (point 5 in Fig. 6), and similarly seven mutations (chimpanzee) compared with one (macaque) in 30 m.y. (point 11 in Fig. 6). When two lineages arising from the same point differ in their rate of fixation in this way it is self evident that both cannot have the same rate as their common stem and so, apart from differences in rate between lineages, there are also changes in the rate of fixation within lineages.

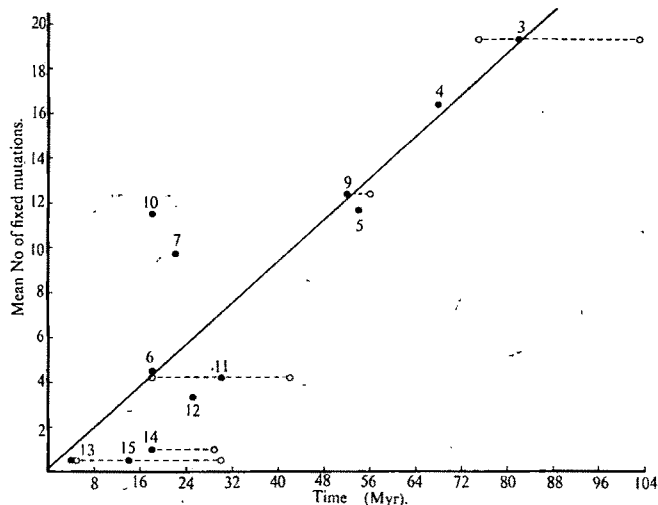


Fig. 7 Relationship between time of divergence and the mean number of fixed mutations in the different lineages since divergence, for eighteen mammal species. Numbered points and possible alternatives as in Fig. 3. The regression of mutations (Y) on time (X) is given by $Y=0.23X+0.10$.

Figure 7 shows the relationship between time of divergence and the mean number of mutations fixed in the different lineages since that time. The wide scatter of points in the region of lower values may be attributable to low mutation values being subject to high sampling errors and to those factors causing differences in rate, both real and apparent, as discussed for Fig. 6. The suspect points of divergence (for example, 10) lie towards the edge of the scatter, whereas differences in rate between lineages arising from one point are more likely to cancel one another out. Thus, point 6, which falls near the fitted line, results from averaging seven mutations (ox) and two (sheep).

The coefficient of correlation for the numbered points in Fig. 7 is 0.89, but this value is spuriously high because each common ancestral stem contributes a constant value towards the total for each of its descendant branches, and numerically lower values are necessarily components of the higher. Bearing in mind this self reinforcement of the data, it can be seen that a regression line fitted to the plotted points suggests a rate of one fixed mutation in about 4 m.y. On the other hand, fluctuations in rate within a lineage can be expected to average out over longer periods of time giving an overall rate for that lineage, and different overall rates can themselves be averaged. As can be deduced from Figs 5 and 6, considering the last 82 m.y., the average rate

for the eighteen mammalian myoglobins is one mutation fixed in 4.2 m.y., whereas the overall rate for the lineage leading to sperm whale is 1 in 3.3, and to macaque is 1 in 6.3. Thus, in the context of molecular evolution we believe that average rate is a more appropriate term than constant rate, and that overall rates for separate lineages are likely to be more informative than the average rate.

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Is the Universe a Vacuum Fluctuation?

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The author proposes a big bang model in which our Universe is a fluctuation of the vacuum, in the sense of quantum field theory. The model predicts a Universe which is homogeneous, isotropic and closed, and consists equally of matter and anti-matter. All these predictions are supported by, or consistent with, present observations.

RECENT observations confirm that the 2.7 K background radiation does indeed have a blackbody spectrum (see refs 1 and 2), which establishes beyond reasonable doubt that some version of the big bang theory is correct. Here I propose a specific big bang model which I believe to be the simplest and most appealing imaginable—namely, that our Universe is a fluctuation of the vacuum, where ‘vacuum fluctuation’ is to be understood in the sense of quantum field theory.

Creation

In any big bang model, one must deal with the problem of ‘creation’. This problem has two aspects. One is that the conservation laws of physics forbid the creation of something from nothing. The other is that even if the conservation laws were inapplicable at the moment of creation, there is no apparent reason for such an event to occur.

The prevailing attitude towards creation is that our Universe is probably undergoing merely one in an infinite sequence of expansions (with intervening contractions). According to this view the Universe has always existed, so its origin lies in the infinite past where it is hopefully not a problem for science.

The preceding viewpoint may indeed be correct, but it leaves unanswered two important questions. First, by what mechanism does the Universe ‘bounce back’ from each contraction? No satisfactory mechanism has ever been proposed. Second, why does the Universe have its particular values for energy, electric charge, baryon and lepton number and so on?

In my model, I assume that our Universe did indeed appear from nowhere about 10^{10} yr ago. Contrary to widespread belief, such an event need not have violated any of the conventional laws of physics. The laws of physics merely imply that a Universe which appears from nowhere must have certain specific properties. In particular, such a Universe must have a zero net value for all conserved quantities.

Conservation

The conserved quantities of physics fall into two categories—discrete and continuous. The discrete quantities are those which characterise elementary particles: electric charge, baryon and lepton number, strangeness and so on. All these quantities have equal magnitude but opposite sign for particles and anti-particles. Hence the discrete conservation laws simply imply that a universe which appears from nowhere must consist equally of matter and anti-matter. Such a possibility is consistent with the properties which have so far been established for our own Universe. (The possibility that our

Universe consists equally of matter and anti-matter has been studied by many authors; for a recent review see ref. 3.)

Of the remaining conservation laws, the most important for cosmology is that concerning energy: although matter and energy can be converted into each other, the net energy remains constant if an intrinsic energy of mc^2 is assigned to each piece of matter.

The Universe has an enormous amount of mass energy, and this might be thought to preclude a creation of the cosmos from nothing. There is, however, another form of energy which is important for cosmology, namely gravitational potential energy. The gravitational energy of a mass m due to its interaction with the rest of the Universe is given roughly by

$$E_g \approx -GmM/R$$

where G is the gravitational constant and M denotes the net mass of the Universe contained within the Hubble radius $R=c/H$, where H is Hubble’s constant.

The density of matter which has so far been observed is somewhat less than the critical value ρ_c required for the Universe to be closed:

$$\rho_c = 3H^2/8\pi G$$

Sandage’s recent determination⁴ of the cosmic deceleration parameter indicates, however, that our Universe probably is closed, in which case the true ρ exceeds ρ_c . If I assume the critical density in my estimate of E_g , I obtain

$$E_g \approx -mc^2/2$$

Hence within a factor of order unity, the negative gravitational energy of any piece of matter is sufficient to cancel the positive mass energy of mc^2 . This naive argument indicates that the net energy of our Universe may indeed be zero.

P. Bergmann has presented a more sophisticated argument which indicates that any closed universe has zero energy. In its simplest form, the argument proceeds as follows (J. M. Cohen, private communication).

Suppose the Universe were closed. Then it would be topologically impossible for any gravitational flux lines to escape. If the Universe were viewed from the outside, by a viewer in some larger space in which the Universe were imbedded, the absence of gravitational flux would imply that the system had zero energy. Hence any closed universe has zero energy.

The preceding remarks indicate that our Universe may have zero net values for all conserved quantities. If this be the case, then our Universe could have appeared from nowhere without violating any conservation laws.

Quantum Field Theory

To indicate how such a creation might have come about, I refer to quantum field theory, in which every phenomenon that could happen in principle actually does happen occasionally in practice, on a statistically random basis. For example, quantum electrodynamics reveals that an electron, positron and photon occasionally emerge spontaneously from a perfect vacuum. When this happens, the three particles exist for a brief time, and then annihilate each other, leaving no trace behind. (Energy conservation is violated, but only for

the brief particle lifetime Δt permitted by the uncertainty relation $\Delta E \Delta t \sim \hbar$, where ΔE is the net energy of the particles and $\hbar$ is Planck's constant.) The spontaneous, temporary emergence of particles from a vacuum is called a vacuum fluctuation, and is utterly commonplace in quantum field theory.

If it is true that our Universe has a zero net value for all conserved quantities, then it may simply be a fluctuation of the vacuum, the vacuum of some larger space in which our Universe is imbedded. In answer to the question of why it happened, I offer the modest proposal that our Universe is simply one of those things which happen from time to time.

One might wonder how a vacuum fluctuation could occur on such a grand scale. My answer is in two parts. The first is that the laws of physics place no limit on the scale of vacuum fluctuations. The duration is of course subject to the restriction $\Delta E \Delta t \sim \hbar$, but this merely implies that our Universe has zero energy, which has already been made plausible.

The second part of my answer lies in the principle of biological selection, which states that any Universe in which sentient beings find themselves is necessarily hospitable to sentient beings. I do not claim that universes like ours occur frequently, merely that the expected frequency is non-zero. Vacuum fluctuations on the scale of our Universe are probably quite rare. The logic of the situation dictates, however, that observers always find themselves in universes capable of generating life, and such universes are impressively large. (We could not have seen this universe if its expansion-contraction time had been less than the 10^{10} yr required for *Homo sapiens* to evolve.)

In summary, observations imply that a big bang occurred about 10^{10} yr ago. One might suppose that the Universe has always existed, undergoing periodic expansions and contractions. There is, however, no known mechanism by which the Universe might bounce back from a contraction. Furthermore, to assume the Universe is infinitely old is to evade, rather than illuminate, the issues of its origin and quantum numbers.

I assume the Universe to be undergoing its initial expansion, evidently having appeared as a fluctuation of the vacuum. The conservation laws of physics then imply that our Universe has the quantum numbers of the vacuum, including zero energy. Hence our Universe must be homogeneous, isotropic and closed, and must consist equally of matter and antimatter. All these predictions are supported by, or consistent with, present observations.

My model is admittedly speculative, and is still in an early stage of development. Quantum theory does, however, imply that the vacuum should be unstable against large scale fluctuations in the presence of a long range, negative energy, universal interaction. Gravitation is precisely such an interaction, so I am encouraged to believe that the origin and properties of our Universe may be explicable within the framework of conventional science, along the lines indicated here.

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Peace Research and SIPRI

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Peace research only began in earnest twenty years ago and the Stockholm International Peace Research Institute was founded as recently as 1966.

IN 1945, Einstein said that the atomic bomb "may intimidate the human race into bringing order into its international affairs, which, without the pressure of fear, it would not do". Einstein was wrong. He did not anticipate that the human race would become rapidly inured to the danger of its own destruction. Twenty years later President Kennedy, seriously alarmed by the general antipathy to the dangers inherent in the deployment of tens of thousands of nuclear weapons, warned that the greatest risk of a general nuclear war—by then capable of eliminating human life on the Earth—was not through calculated intention, but through miscalculation, madness or accident. This year, events during the fourth Middle East war dramatically demonstrated both the truth of President Kennedy's sombre statement and the degree of disorder now existing in international affairs.

Clearly, neither the United States nor the Soviet Union actually desires a nuclear confrontation. And yet the indication that Soviet troops might have been on the way to the Suez Canal led to a world-wide American military alert. The Soviet leaders' miscalculation of the possible American reaction and the American President's actual over-reaction (how

much influenced by domestic political events we will probably never know) to the Soviet move brought the world to the edge of the thermonuclear abyss for the second time in a decade—the Cuban missile crisis being the first. And this nuclear confrontation occurred during a period of *détente*. Can it be reasonably doubted that in some future nuclear confrontation, one or other side will not be deterred by, or will seriously misinterpret, the other's moves? What will happen if a future crisis in a tension area occurs when both leaders of the great powers are severely stressed by domestic pressures? And how much more likely will nuclear war by miscalculation, accident or madness become when many more than the present five countries have nuclear weapons? Is it not apparent that disorder in international affairs will continue to increase unless steps are taken to reverse the trend?

Peace Research

Concern over the consequences of increasing disorder in international affairs and the consequent increase in violence, of the increasing role of military force in international relations, of the increasing probability of nuclear holocaust, of the increasing inhumanity of conventional weapons and methods of warfare, and of the increasing dangers inherent in the world's arms races are some of the objective factors which motivate scientists to work on peace research.

By far the major part of today's science and technology is funded from military expenditures. The importance attached

by states to military strength leads to a massive investment in military research and development, an investment much greater than that put into research and development for peaceful purposes. By comparison with military spending, the resources devoted to understanding the reasons for, and the nature of, international conflicts are minute. So minute, in fact, that many scientists are unaware of the existence of peace research, let alone the results of this research.

The origins of peace research can be traced back to two main sources—the work of the American Quincy Wright on the nature of war and that of Lewis Richardson, a British meteorologist, who developed in the 1930s (although his work remained virtually unknown until 1960) a remarkable mathematical theory of the international system and arms races. It was, however, only about twenty years ago that peace research really began to get under way. The relative infancy of the discipline is shown by the fact that it was not until its 1973 conference at Montreal that the International Political Science Association decided that the time had come to establish a peace research committee to define the subject and to coordinate activity within the field.

Scientists working in peace research generally belong to one of two groups. One group argues that the existing international system, based on a large number of sovereign states, is inherently unstable and will inevitably lead to increasingly severe conflicts and probably eventually to the nuclear destruction of mankind. The only solution, therefore, is to create an entirely new system. Insofar as this group studies the present international system at all, it is to find ways of radically changing it. Research, therefore, focuses on the development of a body of theories and models both about the present international system in an attempt to pinpoint the weaknesses of it and, more often, about possible new international systems which, so it is hoped, will be more stable and less costly. To this end, very complex theories have been developed and analysed, based on game theory, communications theory, systems analysis, cybernetics and so on.

The second group takes the present international system for granted and attempts to discover how it works, to suggest ways of operating it more successfully. It is assumed that by the application of traditional methods—multilateral and bilateral negotiations between states, the development of international law, the United Nations, high level diplomacy and so on—the international system can be made to evolve into an increasingly stable and thus more peaceful system, provided only that the political will to achieve this end exists. The increasing interdependence of states, for example, is seen as an inevitable result of the natural evolution of the present international system. The development of the international system will come about mainly through the efforts of the world's policy makers, who in turn will be influenced by that small group of persons who mould public opinion. And it is, therefore, to the policy makers and the moulders of public opinion that the second group of peace researchers aim the results of their research.

The procedure adopted is to identify, in general terms, those areas in which policy makers could bring about beneficial changes in the international system. Which problems is it politically realistic to expect policy makers to deal with at a given time, bearing in mind the present state of international relations? What are the consequences if a given problem is not solved? With which objectives in mind should particular changes be made to produce the most beneficial effects?

Both approaches to peace research have undoubtedly produced valuable insights into ways of increasing world stability, of improving social justice and of decreasing violence.

Stockholm Institute

The work of the Stockholm International Peace Research Institute (SIPRI), founded in 1966 by the Swedish Parliament to commemorate Sweden's 150 years of unbroken peace, is

entirely within the second of the two categories described above. The established international system is accepted as the framework in which research problems are chosen. No other types of systems are considered. The research is problem oriented and mainly aimed at directly influencing policy makers in current international politics and leaders of public opinion.

An eight-member international governing board is entirely responsible for the operations of SIPRI, even though it is financed by the Swedish Parliament. In the early days, the board decided that the work of the institute should initially concentrate on the problems arising from armaments and disarmament. These were, and still are, considered to be the most serious and urgent of the world's problems. It was soon apparent to the first director of the institute, the British economist Robert Neild, that the most urgent requirement of policy makers in the field of disarmament was relevant data, objectively presented and analysed by an international group of scientists, particularly on the scientific and technical issues involved in disarmament. All of the participants at, for example, the Conference of the Committee on Disarmament (CCD) in Geneva, the main international forum for disarmament negotiations, were, and are, in need of such information, although the delegates of the smaller powers, who generally lack scientific advisers, have the greatest need. The institute, therefore, began by collecting and publishing data on armaments and on developments in military technology, and by analysing ongoing disarmament and arms control negotiations.

One of the first subjects studied in depth at SIPRI was chemical and biological warfare (CBW). In 1964 a group of microbiologists, seriously concerned about the problems of biological warfare and the consequences of the possible military uses of new advances in biology, began meeting as a Pugwash Study Group. It soon became evident that there was a need for a more intensive study than this group could hope to achieve by occasional meetings; SIPRI, therefore, decided to undertake a major review of biological warfare but the study was soon extended to cover chemical warfare as well. The work led to the publication of a six-volume study, *The Problem of Chemical and Biological Warfare*, dealing with the historical, technical, military, legal and political aspects of CBW and possible disarmament measures.

Another subject taken up for study was the trade in major weapons—ships, aircraft, tanks and missiles—between the developed and the non-developed countries during the period after the Second World War. Although the international trade in arms had received much attention in the 1930s, it had been largely ignored in the post-war period. A main aim of the SIPRI study was to propose measures to limit this important element of the global arms race.

When the Partial Test Ban Treaty, prohibiting nuclear weapon tests above ground, was signed in 1963 no agreement was reached on the means of verifying a ban on nuclear tests underground. The main stumbling block was whether seismic verification at long range was alone sufficient. The rate of underground nuclear testing increased considerably after the treaty was signed and, in 1968, SIPRI decided to assemble a group of seismologists to examine the advances in techniques of seismic verification and to see what could be accomplished.

Until 1968, it had been generally assumed that it was impossible to distinguish between the seismic signals generated by earthquakes and explosions. If on past experience an event detected on seismographs was probably not an earthquake and was at a shallow depth, then an explosion was suspected. Analysis therefore consisted of diagnosing earthquakes and eliminating them, leaving a small residue of dubious events. At the expert group meeting, however, it was accepted for the first time, by leading seismologists from ten countries (East and West), that signals generated by explosions could, by analysis of their component waves

be distinguished from the signals generated by earthquakes. Underground nuclear explosions could be thus identified as well as detected. This advance put an entirely new complexion on the possibilities of seismic verification.

The group reported that, with the Western seismic network then existing (which was not specifically designed for detecting underground nuclear explosions) identification down to 20 to 60 kton exploded in granite could be made. But with better equipment (now available) this level could be reduced to 10 kton in granite and, with a wider distribution of sophisticated instruments, the group foresaw the possibility of identification within a range of 2 to 10 kton in granite. The seismic group report, updated in 1970 and 1971 by two progress reports, has had a considerable influence on the ongoing negotiations for a comprehensive nuclear test ban.

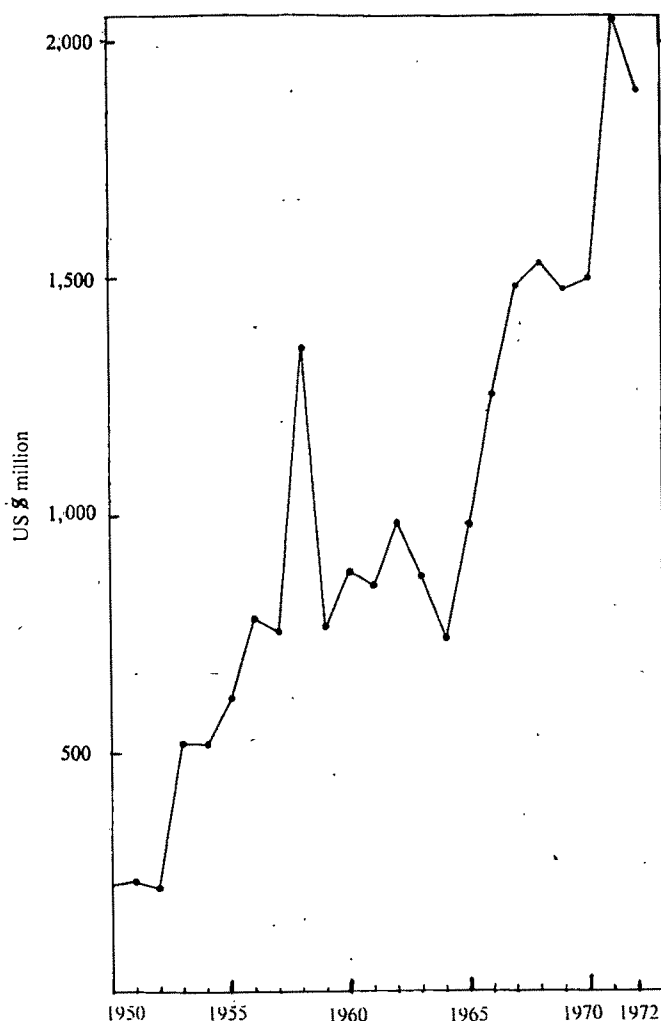


Fig. 1 The arms trade in major weapons between developed and underdeveloped countries 1950-72. (Figures in constant 1968 prices.)

The success of this enterprise led to the formation, in 1971, of another expert group to assess techniques for the inspection of the production of organophosphorus compounds to assist negotiations for a ban on the production of chemical weapons. Once again, the information in the reports arising from these discussions has been used during the negotiations for a CW treaty. The institute is now widening its study of verification issues and is, for example, investigating the potential of established and new technologies for the verification of a range of possible disarmament treaties, up to and including general and complete disarmament.

A third expert group was assembled last June to discuss the military consequences of the spread of peaceful nuclear technology, with particular reference to the issues likely to be raised at the 1975 conference which is to review the operation of the non-proliferation treaty. Is the safeguards system established by the treaty to detect diversion of nuclear material from peaceful to military uses operating satisfactorily? What are the military consequences of new developments in nuclear technology? Does the treaty encourage international cooperation in the development of peaceful nuclear technology to the extent envisaged? Should peaceful nuclear explosives technology be actively developed? If so, under what international regime should this technology be operated? These questions will be dealt with in a two-volume publication; also included will be a set of proposals for the NPT review conference.

The scientists working at SIPRI come from a wide range of social and political backgrounds. Nevertheless, there is general agreement amongst them that the onward rush of military technology will sooner or later produce a catastrophic war and that the only way to eliminate this possibility is by far-reaching disarmament measures. General and complete disarmament is regarded as a politically realistic goal which should be energetically pursued by the world's political leaders. These views are reflected in the SIPRI yearbooks—yearly publications of reference material on world military expenditures, the arms trade, domestic arms production, the nuclear and conventional arms races, current disarmament negotiations and topical issues on armaments and disarmament. The fifth yearbook, to be published next June, will complete the publication of available data on the trade of major arms between the developed countries and ninety-five underdeveloped countries, the arms trade between developed countries, and domestic defence production in developed and underdeveloped countries. The yearbooks are also comprehensive sources of information on bilateral and multilateral disarmament negotiations in all forums.

What general conclusions can be drawn from the activities and publications of SIPRI? In the early 1960s, the decision was taken to abandon attempts to negotiate directly general and complete disarmament and to work instead for so-called partial arms control measures. The theory was that, by this method, it would be possible to move towards general disarmament by small steps. But, even though there have been seven multilateral arms control treaties negotiated since that time, there has been very little progress towards actual disarmament. In addition to the multilateral treaties there have been a number of bilateral agreements between the United States and the Soviet Union. The most important and well known of these are the SALT (Strategic Arms Limitation Talks) agreements—a treaty to limit antiballistic missile systems and an interim agreement on certain measures with respect to the limitation of strategic offensive arms. The political significance of these agreements between the two great powers is considerable but they have been over-advertised as disarmament measures. In fact, both agreements allow quantitative increases in the present level of nuclear weapons since higher ceilings have been established. More seriously, the number of nuclear weapons carried by each missile is allowed to increase unhindered. And there is no limitation at all on the qualitative development of any strategic weapon systems or, for that matter, of any other armaments. For these reasons the SALT agreements can even be regarded as legitimising and encouraging military technological advances. One positive and important disarmament aspect of the SALT agreements concerns the problem of verification. It is noteworthy that the problem of verification, which has plagued all previous disarmament negotiations, was overcome in the SALT agreement, with relative ease. Each party will use its own "national technical means" of verification, chiefly reconnaissance satellites, to provide assurance of compliance.

Prospects for Disarmament

Disarmament in the true sense of the word seems to be fast becoming a dead issue. Even the two obvious next steps, a comprehensive test-ban treaty and a chemical weapons treaty, are unlikely to be soon negotiated. And the current SALT negotiations and the discussions on mutual force reductions in Europe are unlikely to produce far-reaching results for some time to come. Some people are pinning their hopes for further progress on a world disarmament conference. Proposals for such a conference have been made at the United Nations but are stalled by the unwillingness of China to participate. There is, however, reason to assume that China is willing to discuss measures of actual nuclear disarmament given a reorganisation of present negotiating forums. A world disarmament conference could put new life into disarmament discussions. But in itself it would not solve the present problems. The basic requirement is that the nuclear-weapon powers genuinely desire to abolish all weapons of mass destruction as a first step to general disarmament. Once the political will exists, the forum for negotiation is irrelevant.

The recognition of the difficulties of negotiating significant disarmament agreement by the partial-measure approach has led to considerations of other methods of reducing the scope and effect of military operations. One such alternative is the attempt to prohibit firstly the use of unnecessarily cruel and indiscriminate weapons and secondly acts of warfare

directed against the civilian population. The Hague Conventions of 1899 and 1907 prohibit, for example, the use of dum-dum bullets. And the Geneva Protocol of 1925 prohibits the use of gas and other chemical agents and bacteriological agents. But, since these early treaties, enormous improvements have been made in the effectiveness of weapons to kill and maim soldiers and civilians. Initiatives are now being taken to modernise the laws of war to take into account the advances of military technology. For example, the problem of the use of napalm and other incendiary weapons has been put on the agenda of the United Nations. And the Red Cross is considering the possibility of prohibiting the use of a wide range of antipersonnel weapons including high-velocity bullets (which produce wounds similar to dum-dum bullets) fragmentation weapons, etc. The Red Cross may also soon consider such indiscriminate methods of warfare as the terror bombing of civilians, the large scale destruction of food crops, the deliberate flooding of extensive areas and so on. To assist these important initiatives, SIPRI is undertaking a major study of incendiary weapons and weapons which produce effects similar to those which are already banned by international law.

To some extent the lack of progress towards disarmament has disillusioned some of the researchers specialising in the subject. But the great majority are working on, convinced that if the awesome consequences of the increasing militarisation of the world can be made widely enough known the policy makers will have to act.

Comet Kohoutek

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Although comet Kohoutek has not lived up to some of the more extravagant claims made for its astronomical prominence, Professor Biermann shows that observations will still be fruitful because so little is known about the nature of comets.

COMET Kohoutek was discovered on March 7, 1973, near the orbit of Jupiter with a magnitude $m=16$ (or somewhat brighter); an earlier picture was subsequently found on a plate taken on January 28, 1973, at which date the comet was at a heliocentric distance around 5 AU and also of magnitude about 16. The near-parabolic orbit (eccentricity between 0.9999 and 1) was found to have an inclination of 14.3° with a perihelion distance of only 0.14 AU. A comparison with other comets with similar perihelia and similar brightness at large distance from the Sun led to the prediction that near perihelion (which will be passed on December 28, 1973) comet Kohoutek should become at least as bright as Venus, possibly being visible in full daylight.

Comets which, like comet Kohoutek, approach the Sun for the first time, after spending the past 4.5×10^9 yr most probably in the outer fringes of the Solar System, are generally considered to be the oldest essentially unchanged specimens of the products of condensation in the solar nebula, which nearer to the Sun led to the formation of the terrestrial planets or, at somewhat larger distances, of the major planets. For this reason such comets are likely to provide important clues about the very early history of the Solar System and the way in which it formed from collapsing interstellar matter.

The almost star-like central condensation of light seen on plates taken with long-focus instruments, when a comet is far from the Sun and the coma is only weak, is photometrically similar to light from a planetary body¹. To the extent that the influence of the phase function can be neglected (for example, around opposition), the brightness is given essentially by the product of the albedo (A) and the cross section of the nucleus. This cross section, measured for many recent comets by Roemer, was of the order of one or a few km^2 only, the giant in her list of 1956 being comet Humason (1962 VIII), approximately 200 km^2 . For the recent comet Bennett a value of roughly 30 km^2 may be derived from her measurements (see Delsemme²). For comet Kohoutek, measurements made

earlier this year indicate a value of the product of A and cross section about four times that pertaining to comet Bennett, indicating that comet Kohoutek is intermediate in its intrinsic size between comet Bennett and comet Humason, but perhaps more similar to comet Humason. The latter comet, however, already displayed a gas tail at the distance of Jupiter and little dust, whereas comet Kohoutek appears to be rather dusty, with no gas (that is plasma) tail having been discovered so far; CN, a constituent of the coma, was observed on October 15, when the comet was at about 1.8 AU from the Sun.

Icy-conglomerate Model

For the purpose of the present discussion I have adopted in essence the hypothesis embodied in the icy-conglomerate model². At present the most convincing reason for doing so is the fact that in those cases in which the mass of dust released was quantitatively determined (at solar distance of order unity), it was found to be similar to the gas output. Since these comets were rather dusty, it seems likely that for most comets there is even more gas released than dust. This strongly suggests that the gas is present in the central parts of the coma in the form of ice, presumably in a single block. It is of course true that figures for the dust and the integral gas production are so far available for only very few comets. The resulting diameters are again of the order of 1 to 10 km. This means that, barring very exceptional circumstances, the cometary nuclei cannot be seen as disks of finite angular extent, and the ultimate proof that the nucleus of a typical comet is really a single body made up of ice and dust can only be provided by a space mission towards the comet. Such missions are under discussion, but none has been scheduled so far.

Under these circumstances the observations of comet Kohoutek are likely to provide another value for the ratio of gas to dust, but no ultimate answer to the question of the constitution of the cometary nuclei.

Comet Kohoutek will, however, be the first comet to be observed with adequate instrumentation in almost every important range of wavelength. Observations in the ultraviolet have been made over the past three years of comets Tago-Sato-Kosaka, Bennett, Encke and Toba, and such observations will also be made of comet Kohoutek. They should reveal the extent of the hydrogen coma and the amount of hydrogen released per second. They should furthermore reveal the amount of hydroxyl (OH) molecules, which may then be compared with the amount of hydrogen to find out what fraction of the atomic hydrogen may be ascribed to the dissociation of ordinary water molecules. At solar distances less than about 2 AU it is possible, for reasons that are not at all obvious, that ordinary water will turn out to be the main parent molecules of the hydrogen atoms. Comet Kohoutek is a genuine new comet which must have come from a distance of the order of 10,000 or several tens of thousands of AU, whereas comet Bennett was in an orbit of revolution period less than 2,000 yr. Comet Tago-Sato-Kosaka, on the other hand, was also a newcomer, though less dusty than comet Bennett. In comet Kohoutek a dust halo was seen at a distance from the Sun at which ordinary water would have effectively no vapour pressure. The dust particles seen at $\geq 10,000$ km from the cometary nucleus must therefore have been thrown off by some more volatile gas, the simplest alternatives being methane (CH_4), carbon monoxide (CO) and formaldehyde (H_2CO), or possibly ammonia (NH_3). Methane and NH_3 are chemically the most stable compounds in a hydrogen-rich atmosphere at low temperatures; CO, on the other hand, is by far the most abundant molecule in interstellar clouds, with the exception of molecular hydrogen (H_2). The properties of the cometary plasma suggest that neutral CO

should also be relatively abundant in comets⁴. The question whether the chemically most stable molecules— H_2O is of course also in this class—make up most of the cometary ices, or whether molecules such as CO and H_2O are present in appreciable quantities, is evidently of fundamental importance for the chemistry of comets.

Carbon monoxide molecules can be detected in three different spectral regions: in the microwave range at 2.6 mm, in the infrared at 4.6 μm for instance, and with greater difficulty in the ultraviolet. Attempts to detect CO, particularly in the first two wavelength regions mentioned, will be made for comet Kohoutek by several groups in the United States and elsewhere. The observations of CH , will be made using aircraft flying at above 40,000 foot. A transition near 3.3 μm seems most promising.

It is unfortunately conceivable that most of the volatile material in the surface layers will evaporate before the comet comes within 1 AU or less of the Sun, during which time most of the observations are scheduled to be made. For this reason the outcome of these attempts is somewhat difficult to predict, and in any case the search for volatile substances should begin as early as possible. After perihelion passage, the chances may be even worse.



Fig. 1 Photograph of Comet Kohoutek taken at the Royal Greenwich Observatory. On the same scale, the diameter of the Full Moon would be 5.4 cm.

In the radiofrequency range, searches will be made for a number of molecules, in particular formaldehyde at 6 cm, the so-called X-ogen (at 3.3 mm) and OH at 18 cm. The search for the X-ogen molecules, evidenced by an unidentified transition at 89,190 MHz observed so far in about ten interstellar clouds, is of particular interest for the following reason. An identification which seems promising at present is that with the ion of the radical HCO, which occurs in hydrocarbon flames and would be expected to be produced by the (exothermic) reaction of CO ions with molecules containing hydrogen. Bright comets generally show a well developed plasma tail, usually containing many CO ions, and so large numbers of such ions are probably present in comet Kohoutek. If the X-ogen transition were to be observed in comet Kohoutek, the identification mentioned—at this stage only one of several possibilities—would be considerably strengthened.

It goes without saying that observations in the ordinary optical range similar to those which have been made in the past for most bright comets are planned all over the world. Surface photometry of the dust tail, if carried out over a large part of the orbit within 1 or 2 AU, will make it possible to derive both the production rate of dust particles

and the integral gas production, as mentioned already. The technique was developed to a high degree of perfection by Finson and Probst⁵ after the appearance of the two bright comets of 1957. From the isophotes it is possible to derive the initial velocity of the dust particles with respect to the cometary nucleus, that is, the velocity (of the order of 100 or a few hundred metres per second) which the dust particles gain from the drag of the gas which streams out from the surface by evaporation. The analysis shows that this velocity is gained relatively close to the nucleus, because the flux of gas molecules decreases approximately as the inverse square of the distance. In this way the mass flux of the gas can also be determined and has been found to be of the order expected from the absorbed solar radiation and the surface of the comet. The albedo of the cometary nucleus is one of the parameters to be determined; recent work by Delsemme² suggests that the value of the albedo is considerably larger than has generally been assumed until recently, say of the order of several tens of per cent, but reliable values are not yet available. In dusty comets part of the solar light is absorbed before reaching the nucleus to an extent which is difficult to determine, and in addition there are of course dust particles of different sizes for which the ratio of the light pressure to gravity varies with the inverse radius. Comet Kohoutek will provide an excellent opportunity to gain further insights into these rather complex problems.

The only constituent which is at least in some measure representative of the bulk gas production and which is observable in the ordinary optical range is atomic oxygen. The transition in question is the red night sky line which has been seen in almost every bright comet, though accurate photometry has never been carried out owing to the difficulty of separating it from the background. This can be done using the Doppler shift, and it should not be too difficult in the case of comet Kohoutek. The transition probability for this (forbidden) line is so low that photo-excitation would be quite insufficient to explain the observed intensities. The answer to this problem seems to be that the excitation occurs in the process of dissociation or dissociative recombination, which leads to the appearance of the oxygen atom. It is to be hoped that for comet Kohoutek an accurate photometry of the red [OI] line will shed further light on these problems.

The emissions of the neutral molecules and radicals C_2 , C_3 , CN and OH are important in providing clues about the nature of their parents. If their source turns out to be essentially the nucleus itself—they could be contained in ordinary ice in the form of clathrate as suggested many years ago by Delsemme and Swings⁶—the density would, for constant velocity of outflow ($\approx 1 \text{ km s}^{-1}$), vary as the inverse square of the distance from the nucleus, whereas the projected density would vary as the inverse first power of the distance. The expected dissociation at distances between several tens of thousands and several hundreds of thousands of kilometres from the nucleus would give rise to an exponential term and under such simple circumstances the scale distance of the dissociation could be derived from the observations. In principle, it is obviously possible to derive also the scale distance pertaining to the parent molecules, provided that the observed molecule does not emanate from the nucleus itself as suggested above.

In reality such measurements are very hard to make with sufficient accuracy, and it looks as though measurements from space vehicles yield a superior accuracy because of the background effects which are difficult to remove in measurements made from the ground. The fact that for comet Kohoutek such measurements can be planned sufficiently ahead of time, and that the expected brightness of the comet makes the background problems less serious, justifies the hope that the observations of comet Kohoutek will be a major step in the further elucidation of these problems.

The case of the hydroxyl (OH) radical is special for two reasons. First, because its parent is most probably ordinary water which for obvious reasons cannot be observed from the ground and, second, because the emission is so close to the ozone limit that measurements from space vehicles are probably superior.

Plasma Tails

The plasma tails of comets are of particular interest for several reasons. As was recognised long ago, the rapid motion away from the Sun is due to the transfer of momentum from that component of the Sun's corpuscular radiation now called the solar wind. The details of this interaction are not yet sufficiently well understood, particularly because the magnetic fields embedded in the solar wind are likely to play a decisive role. Theoretical work on these questions has long been in progress and leads to the idea that a bow shock and a kind of contact surface should exist around a comet. Without good new observations, however, it will not be possible to arrive at a full understanding of the problems of the plasma flow around and near a comet. For this reason plans have been made to observe comet Kohoutek at intervals of, say, a quarter or a half an hour at stations of different longitude, so that a continuous record over an appreciable fraction of a day is obtained. To ensure the success of such a programme, it is necessary not only to overcome periods during which observing conditions are poor, but also to gain the cooperation of observatories located on adjacent longitudes separated by not much more than 15° since the comet will be observable from any one station only for about an hour, because of its small elongation angle from the Sun (30° to 40°).

Although such observations will yield valuable information on the dynamical processes occurring in the tail, the origin of the tail plasma can be investigated only by observing the light of one of the emission lines of the tail ions (CO^+ , CH^+ , N_2^+ , H_2O^+) near the nucleus. Observations of past comets indicate that CO^+ ions are present, at a distance of 10,000 km from the nucleus and with a density $\sim 10^2 \text{ cm}^{-3}$ (ref. 8). For some comets the observations suggest (though not unambiguously) that the tail ions originate still closer to the nucleus, where ion-molecular reaction and dissociative recombination should limit their lifetimes to a fraction of an hour only. For this reason spectro-photometric work (with adequate resolution to overcome the dust continuum) on the emission of ions close to the nucleus is envisaged.

The number and scope of the observing programmes planned for the coming months are very much larger than could be described in this short article, which represents only a very personal selection. For a much more complete survey of existing programmes reference is made to a report prepared on behalf of Commission 15 of the International Astronomical Union at Goddard Space Flight Center by J. C. Brandt, J. Rahe and V. Vanysek.

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Sea Sediments, Cosmic Rays, and Pulsars

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Measured variations in ^{10}Be and ^{26}Al in deep sea sediments may result from increases in the local cosmic ray intensities produced by a nearby supernova explosion.

MEASUREMENTS of time variations in the local cosmic ray intensity can provide significant information on the origin and propagation of cosmic rays. Long-lived radioisotopes produced by cosmic ray interactions in the Earth's atmosphere offer the best opportunity for studying the time dependence of the cosmic ray intensity¹.

The principal long-lived radioisotopes² produced by cosmic rays in the atmosphere are ^{10}Be and ^{26}Al with mean lives against decay of 2.3×10^6 yr and 1.1×10^6 yr respectively³. ^{10}Be is produced principally by spallation of nitrogen by cosmic ray protons, and ^{26}Al by spallation of argon. These isotopes are quickly precipitated from the atmosphere; however, their latitude dependent production rates are destroyed by ocean current mixing². They are deposited in deep sea sediments in times of the order of 10^3 yr at rates proportional to their global average production values⁴. The production rate of these isotopes as a function of time in the past can thus be related to their present activity as a function of depth:

$$q(t) \propto \tau s A(d) \exp(d/\tau s) \quad (1)$$

where $q(t)$ is the global average production rate (atoms $\text{s}^{-1} \text{cm}^{-2}$ of Earth's surface) at a time in the past, $t=d/s$; d is the depth (cm) in the sediment; s is the sedimentation rate (cm yr^{-1}); τ is the decay mean life (yr) of the radioisotope; and $A(d)$ is the specific activity of the radioisotope (decays $\text{s}^{-1} \text{cm}^{-3}$ of sediment).

Since the production rate $q(t)$ is proportional to the global average cosmic ray intensity, or energy density $w(t)$, then, assuming that the sedimentation rate is constant, the relative cosmic ray energy density may be written

$$w(t)/w(0) \approx \{A(d)/A(0)\} \exp(d/\tau s) \quad (2)$$

where $w(0)$ and $w(t)$ are the global-averaged cosmic ray energy densities at the present and at some time in the past $t=d/s$; $A(0)$ and $A(d)$ are the activities of the radioisotopes in sediment at depths 0 and d . From measurements of the activity of two radioisotopes of different decay mean lives, such as ^{10}Be and ^{26}Al , the sedimentation rate may be directly determined.

Sediment Rates of ^{10}Be and ^{26}Al

The measured activities of both isotopes in the segments of the two deep sea sediment cores are given in Table 1 (refs 5, 6). The sedimentation rate calculated for the ratio of ^{10}Be and ^{26}Al activities in the top and bottom segments of each core is found to be roughly $4 \times 10^{-5} \text{ cm yr}^{-1}$ with an uncertainty

of about $\pm 70\%$ because of the large uncertainty in the ^{26}Al activities. This value is consistent with independent estimates of the sedimentation rate. From the ratio of the specific activity of the ^{10}Be in the upper segments of the cores to the calculated production rate of ^{10}Be in the atmosphere, Yokoyama⁶ found a rate of $3 \times 10^{-5} \text{ cm yr}^{-1}$ with a probable uncertainty of $\pm 50\%$. From the ionium to thorium ratio, Goldberg and Koide⁷ found sediment rates ranging from 3 to $6 \times 10^{-5} \text{ cm yr}^{-1}$ for other South Pacific cores. Similar rates were determined from palaeomagnetic measurements by Ku *et al.*⁸. To study the possible range of the variations in the cosmic ray intensity, we consider two extreme values of the sedimentation rate, 3×10^{-5} and $6 \times 10^{-5} \text{ cm yr}^{-1}$.

Table 1 Activities of ^{10}Be and ^{26}Al in Segments of Two Deep Sea Sediment Cores

	(cm)	Activity (d.p.m. kg^{-1} dry sediment)	
		^{10}Be	^{26}Al
South Pacific core *	0-12	4.7 ± 0.5	0.78 ± 0.34
	12-27	4.6 ± 0.4	
	37.5-52.5	3.6 ± 0.5	0.09 ± 0.18
	52.5-67.5	3.0 ± 0.5	-0.09
	83-110	4.6 ± 0.5	0.3 ± 0.15
North Pacific core *	0-21.5	5.0 ± 0.4	0.9 ± 0.35
	100-120	2.1 ± 0.4	0.1 ± 0.5 -0.1

* The South Pacific core was obtained at $57^\circ 35' \text{ S}$, $174^\circ 15' \text{ W}$ at a depth of 4,760 m; the North Pacific core at $8^\circ 20' \text{ N}$, $145^\circ 24' \text{ W}$ at a depth of 5,110 m.

From equation (2), assuming a constant sedimentation rate, we can calculate the relative global-average ^{10}Be and ^{26}Al production rates as a function of time from the measured activities as a function of depth. The resultant values (Fig. 1) show rough constancy for the last 1 to 2×10^6 yr (depending on the sedimentation rate) preceded by a significant increase between ~ 1.4 and 3.5×10^6 yr ago. This increase is several standard deviations above the constant value and its magnitude ranges from roughly an 80% increase averaged over 0.5×10^6 yr to a 220% increase averaged over 10^6 yr. This increase cannot be due simply to mixing of recent material to depth because the measured ratio of $^{10}\text{Be}/^{26}\text{Al}$ activity differs significantly from that of recent sediment and in fact corresponds to that expected from sediment of between 1.5 and 4×10^6 yr age. Therefore, to account for the increased activity, we must look to either a decrease in the sedimentation rate or an increase in the global-averaged cosmic ray intensity.

If a decrease in the sedimentation rate were responsible for the increase in specific activity, the rate would have to have been less than 30% to 50% of the present rate. It cannot be due simply to removal of sediment. There is no evidence for such time variations in the sedimentation rate but the possibility cannot yet be excluded. Palaeomagnetic measurements of sediment cores made in conjunction with future ^{10}Be analyses will answer this question.

Cosmic Ray Intensity

If the increased activity is due to an increase in the global-averaged cosmic ray intensity, this could in principle be due either to a decrease in the Earth's magnetic field, which at present shields the atmosphere from a significant fraction of the cosmic rays at low latitudes, or to an increase in the local cosmic ray intensity. The possibility that it resulted from a reduction in the geomagnetic field can, however, be ruled out. Even during a field reversal when the field could go essentially to zero, the global averaged intensity² would only increase by about 90%. Since the measured increase in activity ranges from about 80% to 220% depending on the sediment rate, only in the lower limit could the increase possibly be due to a decrease in the magnetic field. Even then, however, the field would have to have remained essentially zero for 0.5×10^6 yr, which is contrary to the wealth of palaeomagnetic evidence⁹.

Thus, if the increase in activity is not caused by a decrease in the sedimentation rate, it must directly reflect an increase in the cosmic ray intensity. Such intensity increases could be expected from nearby supernova explosions if cosmic rays are produced either in the initial explosion or soon after as the pulsar rapidly slows down¹⁰. An estimate of the ages and distances of such supernovae can be made from pulsar observations, assuming that the pulsars are the neutron star remnants of supernovae. From these estimates we can attempt to correlate the apparent cosmic ray intensity increase with a particular supernova. Pulsar ages can be estimated from the measured period P and slowing down rate $\dot{P}$. General considerations¹¹ of the slowing down of neutron stars suggest that the age is between $P/2\dot{P}$ and $P/4\dot{P}$. Pulsar distances can be determined from the dispersion measure of their signals, assuming an interstellar electron density.

Of the 30 pulsars for which both P and $\dot{P}$ have been measured¹² roughly half have ages which lie between 1.4 and 3.5×10^6 yr. Of these, PSR1929 with an age of 1.6 to 3.3×10^6 yr is apparently the closest. It has a dispersion measure of only $3.2 \text{ cm}^{-3} \text{ pc}$. The next closest, PSR2045, has a dispersion measure of 11.5. The interstellar electron density ranges from about 0.1 cm^{-3} in ionised regions around pulsars

to 0.02 cm^{-3} in undisturbed regions¹³. Assuming a mean value of $\sim 0.05 \text{ cm}^{-3}$ gives a mean distance for PSR1929 of $\sim 60 \text{ pc}$ with an uncertainty of probably $\pm 30 \text{ pc}$. Since we are interested not in the present distance but in the distance some 1.6 to 3.3×10^6 yr ago, the unknown relative velocity of the pulsar with respect to the Sun adds an additional uncertainty in the distance at the time of the supernovae explosion when the cosmic rays were produced. Typical relative velocities of the order of $\sim 10 \text{ km s}^{-1}$ would lead to an uncertainty of about $\pm 15 \text{ pc}$ to $\pm 30 \text{ pc}$.

If we assume that the observed activity increase does reflect an increase in the local cosmic ray intensity caused by the supernova explosion of which PSR1929 is the remnant neutron star, we can then ask what cosmic ray total energy releases and what cosmic ray propagation processes are required to account for the magnitude and time dependence of the increase. Coupled with the two values of the sedimentation rate of 3×10^{-5} and $6 \times 10^{-5} \text{ cm yr}^{-1}$ we will consider the two limiting ages of the supernovae explosion of 3.3×10^6 and 1.6×10^6 yr, in both cases assuming a distance of 60 pc.

Cosmic Ray Propagation

Several processes of cosmic ray propagation have been considered¹⁴⁻¹⁶: simple streaming of cosmic rays in the interstellar medium; three-dimensional diffusion, either by scattering of cosmic rays from one magnetic field line to another or by streaming along random walking field lines; or compound diffusion, consisting of one-dimensional diffusion along field lines which random walk in three dimensions. Assuming a statistical distribution of discrete cosmic ray sources in space and time, Lingenfelter and Ramaty¹⁶ found that the measurements of anisotropy and abundance of secondary components (^2H , ^3He , LiBeB) required a mean free path of $\sim 0.1 \text{ pc}$ for cosmic ray propagation by three-dimensional diffusion and $\sim 30 \text{ pc}$ by compound diffusion.

We shall first consider, however, the possibility that the cosmic rays simply stream out radially from the supernova source. If the total cosmic ray energy produced in the source is W_{sn} , then the total cosmic ray increase at the Earth is $W_{\text{sn}}\pi r^2/4\pi d^2$ where r is the radius of the Earth and d is the distance of the source ($\sim 1.8 \times 10^{20} \text{ cm}$). This is equal to $4\pi r^2 \Delta w c T$ where Δ is the relative increase in measured activity, w is the present cosmic ray energy density ($10^{-12} \text{ erg cm}^{-3}$), c is the velocity of light and T is the time interval over which the increase Δ is observed. Thus we see that the required $W_{\text{sn}} = 16\pi d^2 c \Delta w T$. For a sedimentation rate of $6 \times 10^{-5} \text{ cm yr}^{-1}$, the increase $\Delta = 0.8$ and $T = 4.5 \times 10^5 \text{ yr}$, requiring a total cosmic ray energy production in the source $W_{\text{sn}} \approx 5 \times 10^{53} \text{ erg}$ to account for the measured increase in activity. For a rate of $3 \times 10^{-5} \text{ cm yr}^{-1}$, $\Delta = 2.2$ and $T = 9 \times 10^5$, requiring $W_{\text{sn}} \approx 3 \times 10^{54} \text{ erg}$. Both of the values are several orders of magnitude greater than the estimates of 10^{51-52} erg for the cosmic ray energy available in either supernovae explosions¹⁷ or in slowing down of neutron stars¹⁸. Thus, even allowing for the uncertainty in the distance, we conclude that cosmic ray propagation by streaming cannot account for the observed increase in activity.

Much smaller total cosmic ray energies are required, however, for cosmic ray propagation by diffusive processes. The time dependence of the increased cosmic ray energy density $\Delta w(t)$ at the Earth resulting from three-dimensional diffusion of cosmic rays from a nearby source of age t_0 and distance d is

$$\Delta w(t) = W_{\text{sn}} d^{-3} [2\pi(t_0 - t)/3t_m]^{-3/2} \exp\{-3t_m/2(t_0 - t)\}$$

where $t_m = d^2/2\lambda c$ and λ is the diffusion mean free path. Using a λ of 0.1 pc , we have calculated the time dependence $\Delta w(t)$ and normalised W_{sn} to give the observed relative increase in activity. This calculated increase added to a constant background is shown in Fig. 1 for the two sedimentation rates considered. For the rate of $6 \times 10^{-5} \text{ cm yr}^{-1}$ we use the minimum age of PSR1929, $t_0 = 1.6 \times 10^6 \text{ yr}$, and find that the

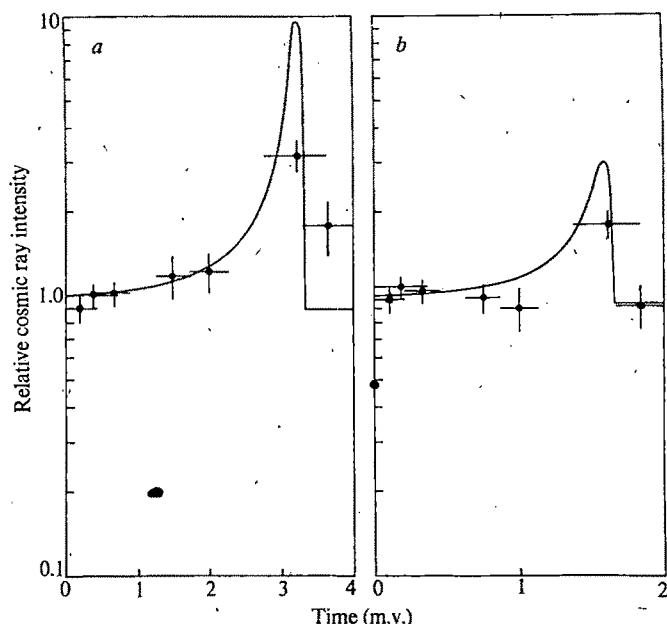


Fig. 1 Relative cosmic ray intensity as a function of time deduced from ^{10}Be activity in deep sea sediments, using two limiting cases for the sedimentation rate: a, $3 \times 10^{-5} \text{ cm yr}^{-1}$; b, $6 \times 10^{-5} \text{ cm yr}^{-1}$. The curve represents the intensity increase expected from the supernova explosion associated with pulsar PSR1929, assuming cosmic ray propagation by three-dimensional diffusion.

measured increase in activity requires a total cosmic ray energy in the source $W_{sn} \approx 1.8 \times 10^{50}$ erg. For the rate of 3×10^{-5} cm yr $^{-1}$ we use the maximum age of PSR1929, $t_0 = 3.3 \times 10^6$ yr, and find it requires $W_{sn} \approx 7.4 \times 10^{50}$ erg. These two values are in good agreement with the estimated cosmic ray energy available in such sources, mentioned above, and suggest that three-dimensional diffusion of cosmic rays from PSR1929 could indeed account for the observed increase in activity. This would require that at the present some 6% to 10% of the local cosmic ray intensity comes from this source. The associated anisotropy would be $< 4 \times 10^{-5}$ which is well below the present upper limit of $< 10^{-3}$.

Calculations of the increase in intensity expected from cosmic ray propagation by compound diffusion with a mean free path of ~ 30 pc give comparable values of W_{sn} and time dependences which are also consistent with the measured values.

There is reason, however, to question the applicability of both of these propagation models at early times near a source, since in both models it is assumed that the cosmic rays do not strongly affect the structure of the magnetic field through which they propagate. This in turn requires that the cosmic ray energy density does not greatly exceed the magnetic field energy density. Though this condition is apparently satisfied in much of the interstellar medium where the mean energy density of the cosmic rays and the magnetic field are approximately equal, it clearly would not be satisfied at early times near a source where the energy density of cosmic rays would necessarily be much greater than that of the ambient magnetic field. The early phase of cosmic ray propagation near a source has received relatively little attention, partly because of the complexity of the dynamical problems involved and partly because of the lack of suitable observations against which to test a model. If the correlation, suggested here, between the measured increase in activity and the supernova which produced

PSR1929 is significant, suitable observations are no longer lacking.

In view of the meagreness of the present data on variations of ^{10}Be and ^{26}Al activity in deep sea sediments this discussion has been highly speculative. But we hope that by pointing out the implications of the existing measurements we shall stimulate others to make further measurements which may either confirm or refute the variations in the cosmic ray intensity which have been suggested.

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Cyclic Nucleotides as Intracellular Mediators of the Expression of Antigen-sensitive Cells

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The interaction of antigen with antigen-sensitive cells can lead to antibody synthesis (induction) or can render these cells non-inducible (paralysis). Cyclic AMP may be the intracellular mediator of a paralytic signal whereas both cyclic AMP and cyclic GMP may be required as mediators of an inductive signal.

THE interaction of antigen with antigen-sensitive cells is required both for the induction of antibody synthesis (induction) and for rendering these cells non-inducible

(paralysis). We wish to discuss here the intracellular signals that may determine whether antigen-sensitive cells follow inductive or paralytic pathways. There is evidence that competition between these two pathways operates at the level of the antigen-sensitive cell itself¹. The delivery of two signals to antigen-sensitive cells leads to the induction of antibody synthesis: one of these signals is delivered through the antigen-binding receptor, the second through the cooperating cell system. In certain conditions bacterial lipopolysaccharides (LPS) can deliver the cooperating cell signal to antigen-sensitive cells²⁻⁴. The signal delivered to antigen-sensitive cells as a consequence of binding antigen appears to be common to both inductive and paralytic pathways. For example, deaggregated human gamma globulin is paralytic in adult mice but can be rendered immunogenic by LPS⁵. Similarly, DNP coupled to a non-immunogenic

polymer (D-glutamic acid-D-lysine) is itself paralytic but induces antibody synthesis when allogeneic lymphoid cells are used to provide the cooperating cell signal⁶. These experiments suggest that the interaction of antigen with receptors on antigen-sensitive cells leads to the paralytic pathway and that the cooperating cell signal diverts cells receiving the antigenic signal from a paralytic to an inductive pathway.

Many membrane-mediated events are coupled to an enzyme, adenylyl cyclase, which rapidly increases the intracellular concentration of adenosine 3',5'-cyclic phosphate (cyclic AMP)⁷. Several studies indicate that cyclic AMP directly affects the division of cells. High intracellular levels have an antimitotic effect on cells, and agents which stimulate confluent, normal cells to resume division decrease the intracellular levels of cyclic AMP⁸⁻¹¹. The addition of exogenous cyclic AMP to culture cells often results in the expression of a specialised function characteristic of the cell type. In neural tumours, cyclic AMP induces neurite formation¹²; in hepatomas, tyrosine transaminase^{13,14}; in melanomas, pigment production^{15,16}; and in lymphomas, cell death¹⁷. These findings suggest that cyclic AMP is an intracellular mediator of a programmed cell function and that increasing intracellular levels of cyclic AMP induces specialised cells to express their programme.

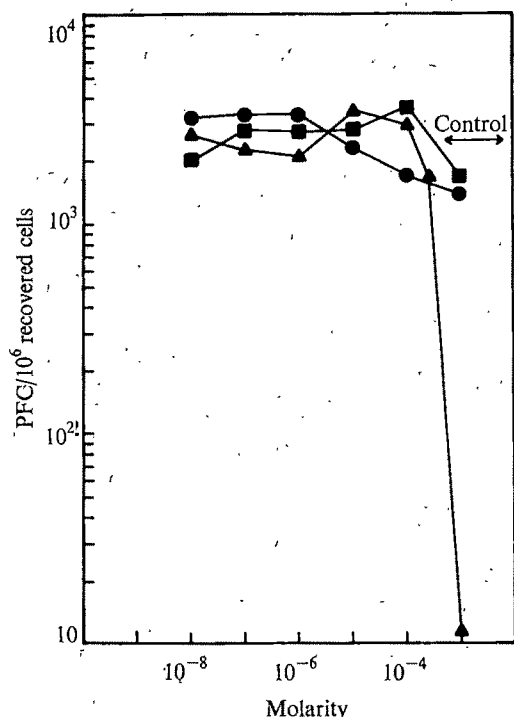


Fig. 1 Effect of different concentrations of dibutyryl cyclic AMP (▲), adenosine (AdR, ●) and adenylic acid (AMP, ■) on *in vitro* primary immune responses to SRBC. Spleen cultures were prepared from C57Bl/6 mice as described before^{2,3}. Each culture contained 1×10^7 spleen cells, 3×10^6 SRBC in 1 ml Eagle's medium, and assayed after 4 d in a microscope slide assay for haemolytic PFC. The control level denotes the PFC in culture lacking cyclic AMP, AdR or AMP. Adenosine N⁶, O^{2'}-dibutyryl cyclic AMP, 2', 3'- and 5' adenylic acids were obtained from Calbiochem.

Extracellular cyclic AMP has been reported both to stimulate¹⁸⁻²⁰ and to inhibit²¹ the induction of antibody synthesis. These studies do not distinguish between cyclic AMP having a general effect on the growth rates of induced antigen-sensitive cells, and cyclic AMP possessing a role in the signal system responsible for the induction process

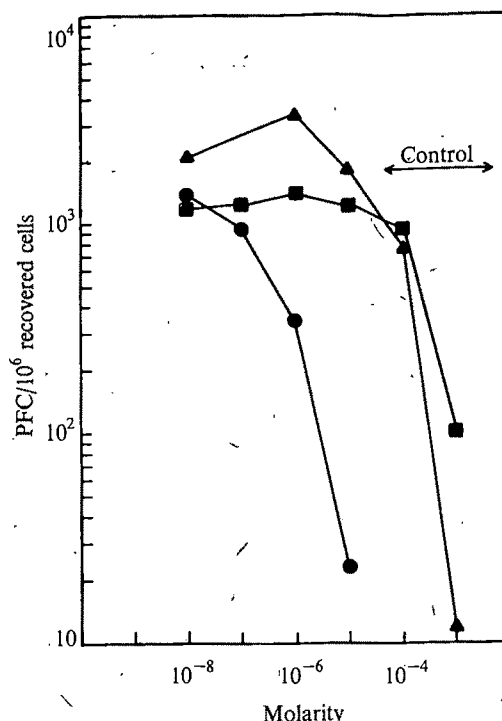


Fig. 2 Effect of theophylline (■) and papaverine (●) on the induction of *in vitro* primary immune responses to SRBC. Spleen cultures were prepared from C57Bl/6 mice and assayed on day 4. The control level denotes the immune response to SRBC in spleen cultures lacking papaverine or theophylline. Papaverine hydrochloride was obtained from S. B. Penick and Company, New York. Theophylline was obtained from Calbiochem. ▲, Dibutyryl cyclic AMP.

itself. We describe here the inactivation of the induction of an *in vitro* IgM response to sheep red blood cells (SRBC) by cyclic AMP and its reversal by guanosine 3',5'-cyclic phosphate (cyclic GMP). Further, in mouse spleen cultures depleted of cooperating activity that do not respond to SRBC, the addition of cyclic GMP permits induction. In view of these experiments as well as our knowledge of the ubiquitous role of cyclic nucleotides as intracellular mediators of programmed cell functions, we suggest that cyclic AMP and cyclic GMP mediate the intracellular signals which determine whether antigen-sensitive cells follow an inductive or a paralytic pathway. Cyclic AMP alone is postulated to mediate paralysis whereas both cyclic AMP and cyclic GMP are required for induction.

Cyclic Nucleotides and Induction

The effect of different concentrations of dibutyryl cyclic AMP on the induction of *in vitro* primary immune responses to sheep erythrocyte antigens (SRBC) in normal (C57Bl/6) spleen cultures is described in Fig. 1. Concentrations of dibutyryl cyclic AMP below 10^{-4} M had little effect on the *in vitro* immune responses to SRBC although some stimulation (two to five-fold) in the response was often observed in the presence of 10^{-5} M dibutyryl cyclic AMP. As the concentration of dibutyryl cyclic AMP was increased in spleen cultures from 10^{-4} M to 10^{-3} M, however, increasing inhibition of the immune response was observed. Both adenylic acid (AMP) and adenosine (AdR) when added to spleen cultures in the same concentration range had little effect on the induction of *in vitro* immune responses. The presence of 10^{-3} M AdR had a slight inhibitory effect (<20%) on the *in vitro* immune response in different experiments.

The experiments described in Fig. 2 compared the effects of theophylline and papaverine on the induction of *in vitro*

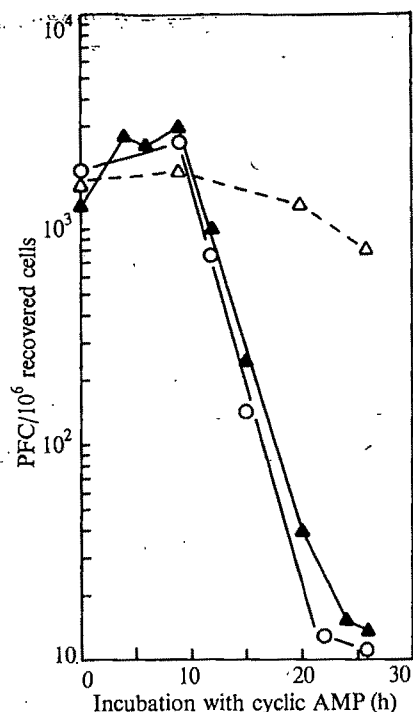


Fig. 3 Effect of time of incubation with cyclic AMP on the induction of *in vitro* primary immune responses to SRBC. Spleen cultures prepared from C57Bl/6 mice were incubated with 10^{-3} M dibutyryl cyclic AMP in the presence (▲) and absence (○) of SRBC for the times indicated. Cultures were then washed and resuspended in fresh Eagle's medium (1 ml). Cultures lacking SRBC were then supplemented with 3×10^6 SRBC. The control cultures (Δ) were spleen cells incubated in the absence of SRBC and dibutyryl cyclic AMP, and at the times indicated washed and recultured in fresh Eagle's medium with 3×10^6 SRBC. All spleen cells were assayed for SRBC-specific PFC 4 d after the start of cultures. For removal of cyclic AMP from cultures, medium containing non-adherent cells was removed gently from each spleen culture and each dish was washed once by adding back and removing a 1 ml sample of fresh medium. The supernatant collected from each culture dish was centrifuged at 850g for 5 min, removed and each cell pellet was resuspended in 1 ml medium and recultured in the dish from which it was originally collected.

immune responses to SRBC. While theophylline at 10^{-3} M inhibited the immune response about ten-fold, papaverine at 10^{-5} M suppressed induction 100-fold (Fig. 2). Since both theophylline and papaverine inhibit phosphodiesterase activity and lead to the accumulation of intracellular cyclic AMP^{22,23}, the inhibition of immune responses observed in these experiments seems to be mediated intracellularly by cyclic AMP.

The kinetics of the establishment of *in vitro* immune unresponsiveness by pulses of 10^{-3} M dibutyryl cyclic AMP is described in Fig. 3. When the extracellular dibutyryl cyclic AMP was removed at various times after the start of spleen cultures, two effects were observed. First, when removed up to 9 h after addition to spleen cultures, there was characteristically a stimulation of the subsequent immune response to SRBC. This has varied in our experiments from two to six-fold. Second, between 12 and 20 h after addition of dibutyryl cyclic AMP to spleen cultures there occurred an exponential decrease in the subsequent immune response to SRBC. The half-life of the ability to respond to SRBC during this decline was about 3 h. The presence or absence of SRBC during exposure of spleen cells to 10^{-3} M dibutyryl cyclic AMP did not affect the inhibition of immune responsiveness to SRBC (Fig. 3), this possibly being due to the concentration of cyclic AMP used.

The induction of *in vitro* immune responses to SRBC requires collaboration between two types of antigen-sensitive

cells, the bone marrow-derived precursor cell (P-AFC) and the thymus-derived (T) cells. If dibutyryl cyclic AMP inhibited the expression of either or both of these lymphoid cell types the *in vitro* immune responses would be suppressed. Consequently, we have examined the effects of dibutyryl cyclic AMP on the expression of P-AFC and T cells in two ways.

First, a previous finding was utilised to examine the effect of dibutyryl cyclic AMP on P-AFC²⁴. Bacterial lipopolysaccharides (LPS) permit a response to antigen in spleen cultures depleted of T cells. Congenitally athymic (nude) mice are deficient in T cells²⁵. Nude spleen cultures containing SRBC were exposed to 10^{-3} M dibutyryl cyclic AMP for various times, the cyclic AMP then removed and 5 μ g LPS added to the cultures. After 4 d, cultures were analysed for their immune response to SRBC. The results are described in Fig. 4A. When compared with control cultures (nude spleen cells not exposed to dibutyryl cyclic AMP) it can be seen that increasing the length of time

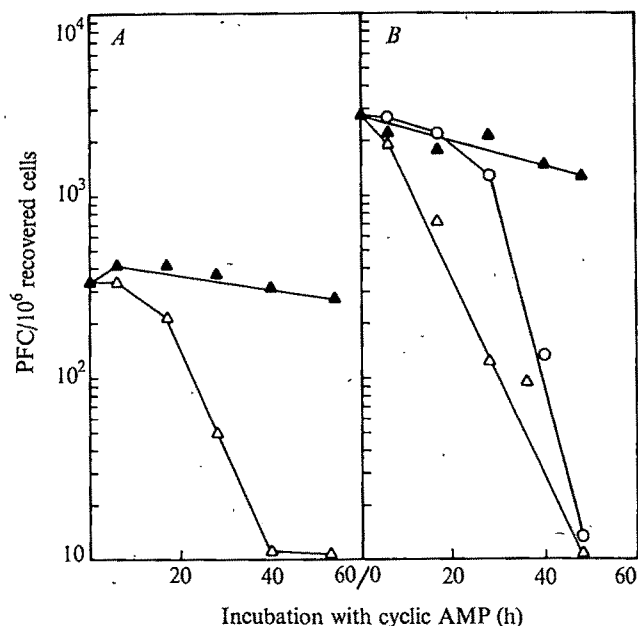


Fig. 4 The kinetics of inactivation of P-AFC and T_{SRBC} cells by 10^{-3} M dibutyryl cyclic AMP. A, Control cultures (▲) containing 10^7 nude spleen cells were incubated, washed and recultured with 5 μ g LPS and 3×10^6 SRBC ($t_i=40$ h); + cyclic AMP (Δ) cultures containing 10^7 nude spleen cells were incubated with 10^{-3} M dibutyryl cyclic AMP for the times indicated, washed and recultured with 5 μ g LPS and 3×10^6 SRBC ($t_i=5$ h). B, Control cultures (▲) containing 10^7 nude spleen cells or 5×10^6 T_{SRBC} cells were incubated without cyclic AMP and washed at the times indicated. The cells from one nude culture were mixed with those from one T_{SRBC} culture, 5×10^6 SRBC added and then incubated another 4 d before assaying ($t_i=38$ h); P-AFC cultures (Δ) containing 10^7 nude spleen cells were incubated with 10^{-3} M dibutyryl cyclic AMP for the times indicated, washed and then recultured with 5×10^6 T_{SRBC} cells which had not been treated with cyclic AMP and 3×10^6 SRBC ($t_i=7$ h); T_{SRBC} cultures (○) containing 5×10^6 T_{SRBC} cells were incubated with 10^{-3} M dibutyryl cyclic AMP for the times indicated, washed and then recultured with 10^7 nude spleen cells which had not been treated with cyclic AMP, and 3×10^6 SRBC ($t_i=3$ h). Mice homozygous for the mutation nude were bred as described elsewhere²⁵. *Salmonella typhosa* lipopolysaccharide (LPS) (Difco) was dissolved in 0.1 M phosphate buffer (pH 8.0) at a concentration of 1 mg ml⁻¹ and boiled for 60 min before use. To prepare T_{SRBC}, C57Bl/6 mice were irradiated (850 r) using cobalt-60 and then injected intraperitoneally with 100 U heparin (Upjohn). After 10 min these irradiated mice were injected intravenously with 0.2 ml of a solution containing $5-10 \times 10^7$ thymus cells from non-irradiated C57Bl/6 donors and 2×10^8 SRBC. After 5 to 8 d the spleen cells were isolated from the irradiated mice and used as the source of activated thymus cells.

of exposure to dibutyryl cyclic AMP decreases the ability of LPS to stimulate SRBC responses in nude cultures (Fig. 4A). From these data the following calculations can be made. The P-AFC in control nude spleen cultures has a background half-life of 40 h as determined by ability to respond when challenged with 5 μ g LPS and SRBC. In contrast, in nude spleen cultures pulsed with 10^{-3} M dibutyryl cyclic AMP, and then challenged with 5 μ g LPS and SRBC, the half-life of the P-AFC is decreased to about 5 h.

Second, these results were extended by comparing the inactivation of P-AFC by dibutyryl cyclic AMP using T cells activated to SRBC (T_{SRBC}) in place of LPS. The rate of inactivation of P-AFC was determined by treating nude spleen cultures with 10^{-3} M dibutyryl cyclic AMP for varying times and assaying the remaining immune response to SRBC by the addition of SRBC and an excess of T_{SRBC} cells. Control nude spleen cultures were treated in exactly the same way except that dibutyryl cyclic AMP was not added to the nude spleen cultures. All cultures were assayed for immune responses to SRBC 4 d after the end of the cyclic AMP pulse period and the addition of T_{SRBC} and SRBC. These data have been plotted in Fig. 4B. The results are similar to those obtained using LPS (Fig. 4A). The P-AFC in control nude spleen cultures had a half-life of 38 h, and in dibutyryl cyclic AMP-treated cultures a half-life of about 7 h.

Table 1 Effect of Cyclic GMP on Induction of Immune Responses to SRBC in Normal (C57Bl/6) and T Cell-depleted (Nude) Spleen Cultures

Concentration of cyclic GMP (M)*	PFC/ 10^6 recovered cells (day 4)		
	C57Bl/6†	Nude†	Nude‡
None added	568	15	21
5.0×10^{-3}	310	116	29
2.5×10^{-3}	376	89	458
1.0×10^{-3}	413	57	496
5.0×10^{-4}	976	29	348
2.5×10^{-4}	571	12	241
1.0×10^{-4}	891	<10	169
1.0×10^{-5}	763	<10	36
1.0×10^{-6}	516	<10	<10
1.0×10^{-7}	617	<10	<10

The results represent the mean of duplicate cultures and are representative of at least four separate experiments. Culture procedures are described in the legend to Fig. 1. Cyclic GMP was obtained from Calbiochem.

* Cyclic GMP added at start of cultures.

† Cultures not fed with cyclic GMP.

‡ Cultures fed daily with 5.0×10^{-4} M cyclic GMP.

The effect of dibutyryl cyclic AMP on the expression of activity in the T_{SRBC} cell population was also determined. Here, cultures containing 5×10^6 T_{SRBC} cells were exposed to 10^{-3} M dibutyryl cyclic AMP* for various times, removed and 10^7 untreated nude spleen cells and SRBC added to each culture. Again, 4 d after the pulse with dibutyryl cyclic AMP cultures were assayed for immune responses against SRBC. When compared with the control cultures (Fig. 4B), it was apparent that dibutyryl cyclic AMP also affected the activity of T_{SRBC} cells. Since in nude spleen cultures containing fresh T_{SRBC} cells, it is the T cells which are in excess, the half-life of T_{SRBC} cells can be determined only when their activity becomes limiting. Thus, T_{SRBC} cells can be assumed to be limiting when the PFC response decreases exponentially. These data indicate that the half-life of T_{SRBC} in the presence of dibutyryl cyclic AMP is about 3 h.

The addition of cyclic GMP to normal (C57Bl/6) spleen cultures in the range of 10^{-3} M to 10^{-8} M had little effect

on the induction of immune responses to SRBC (Table 1). The addition of cyclic GMP to nude spleen cultures containing SRBC resulted, however, in the stimulation of immune responses to SRBC (Table 1). Feeding the cultures with cyclic GMP each day seems to enhance the *in vitro* immune responses to SRBC. Since nude spleen cells are deficient in the cooperating T cell population it seems that the cyclic GMP may be replacing the function of T cells.

Table 2 Effect of Cyclic GMP on Establishing Immune Unresponsiveness by Cyclic AMP

Cyclic nucleotides in cultures *		PFC/ 10^6 recovered cells (day 4)†
Cyclic AMP (M)	Cyclic GMP (M)	
None added	None added	848
10^{-3}	None added	26
10^{-3}	10^{-3}	21
10^{-3}	10^{-4}	525
10^{-3}	10^{-5}	268
10^{-3}	10^{-6}	114

* Cyclic GMP and cyclic AMP were present in spleen cultures prepared from C57Bl/6 mice for the initial 24 h, then cells were washed, recultured in fresh medium and left a further 3 d before assaying.

† Figures represent the mean of triplicate cultures and are representative of three separate experiments. Culture procedures are identical to those described in the legends to Figs 3 and 4.

Treatment of spleen cultures with 10^{-3} M dibutyryl cyclic AMP for 24 h was sufficient to induce immune unresponsiveness. When spleen cultures containing 10^{-3} M dibutyryl cyclic AMP and different concentrations of cyclic GMP (10^{-3} M to 10^{-5} M) were washed and recultured after exposure for 24 hours to these cyclic nucleotides, two effects were observed (Table 2). First, cyclic GMP reverses the inactivating effects of cyclic AMP. Second, there is an optimum ratio of cyclic AMP/cyclic GMP for this reversal. Finally, we should mention that cyclic GMP seems to be better than dibutyryl cyclic GMP in stimulating these various responses (unpublished data). All data reported here have been obtained using cyclic GMP.

Cyclic Nucleotides: Intracellular Mediators

The small number of antigen-sensitive cells in the spleen that respond to any given antigen makes it difficult to analyse the biochemical events associated with the interaction of antigen with cell surface receptors. High concentrations of cyclic AMP inhibit the induction of *in vitro* immune responses; this inhibition is reversed by the presence of cyclic GMP. In the absence of T cells, cyclic GMP induces immune responses. We have based our interpretation of these data on three points: (a) each antigen-sensitive cell can be induced or paralysed¹; (b) the interaction of antigen with the receptor on antigen-sensitive cells leads to the paralytic pathway^{5,6}; (c) induction requires in addition to the signal initiated by the antigen-receptor interaction a second signal initiated by the thymus-derived cooperating system^{3,5,6}.

We suggest that the binding of antigen to receptors on antigen-sensitive cells activates the adenyl cyclase system to increase intracellular levels of cyclic AMP. The increase in cyclic AMP triggers the paralytic pathway. The evidence for this is the finding that high concentrations of cyclic AMP inactivate both P-AFC and T_{SRBC} cells (Fig. 4). A comparison by cyclic AMP inactivation of antigen-sensitive cells, both P-AFC and T cells (Fig. 4), with their inactivation (paralysis) by antigen²⁴, shows several similarities. Although both processes render cells non-inducible, there is a different rate of inactivation for each antigen-sensitive cell type.

At saturating concentrations of dibutyryl cyclic AMP (10^{-3} M) the half-life of the bone-marrow-derived P-AFC is approximately 6 h while that of the cooperating thymus-derived T cell is around 3 h (Fig. 4). In normal spleen cultures, cyclic AMP inactivates the response to SRBC with a half-life of 3 h, showing, as expected, that it is the T cell which first becomes limiting (Fig. 3). These *in vitro* data are in accord with *in vivo* data showing a greater rate of paralysis by antigen of thymus-derived cells as compared with bone-marrow-derived cells²⁴. Further evidence that cyclic AMP is the intracellular mediator of the inactivation process comes from the fact that phosphodiesterase inhibitors, theophylline and papaverine also render cultures unresponsive (Fig. 2). Since similar concentrations of cyclic AMP do not kill other cell types but rather induce such cells to express a differentiated function¹²⁻¹⁷ we believe the cyclic AMP inactivation of antigen-sensitive cells is revealing a differentiated pathway unique to these cells. The ability of cyclic GMP to reverse the cyclic AMP inactivation of antigen-sensitive cells supports this contention (see below).

We suggest that the second signal delivered by the interaction of the cooperating cell system with antigen-sensitive cells activates a guanyl cyclase system to increase intracellular cyclic GMP. Induction requires activation of both adenyl (signal (1)) and guanyl (signal (2)) cyclase systems. The evidence for this is that spleens of nude mice deficient in the thymus-derived cooperating system will respond to SRBC if cyclic GMP is added to the system. Under these conditions signal (1) comes to the P-AFC from the SRBC-receptor interaction and signal (2) from cyclic GMP. The membrane interaction which leads to an increase in the intracellular cyclic GMP level in the P-AFC normally requires a component from the cooperating cell. As far as the P-AFC is concerned, increasing cyclic GMP levels is the first intracellular component of the series of events we call signal (2).

Since the interaction of antigen with antigen-sensitive cells seems to deliver a signal common to both inductive and paralytic pathways, it is a requirement of the above two proposals that the inactivation by cyclic AMP be reversed by cyclic GMP, and this is found (Table 2). Simply reversing cyclic AMP inactivation is insufficient to explain induction because the antigen-sensitive cell would be left essentially in the state it was before encountering antigen. Therefore, cyclic GMP must have a further role. Induction must depend on the simultaneous presence at an effective level of both cyclic AMP and cyclic GMP. In other words, the cell must be able to read the ratios of cyclic AMP to cyclic GMP. It is important to note that there is an optimal ratio for reversal of cyclic AMP inactivation. At a given level of cyclic AMP, concentrations of cyclic GMP higher than optimum lead to a suppression of the response (Table 3). This fact taken as biologically significant implies that when the cooperating activity rises above a given level due to induction, P-AFC programmes for IgM secretion are switched off.

There are agents which interact with lymphocytes to induce proliferation. In the case of the phytohaemagglutinin or concanavalin A-induced proliferation of thymus-derived lymphocytes, optimum mitogenic concentrations of these substances produce rapid ten- to fifty-fold increases in intracellular cyclic GMP while little change occurs in cyclic AMP²⁵. In the case of LPS, its effect on the cyclic GMP level in bone marrow-derived lymphocytes has not yet been measured. These mitogens also affect the immune response so as to either enhance or inhibit. Under the present formulation it is to be expected that agents which affect cyclic GMP levels in the cell would also affect proliferation and induction both positively and negatively.

The closing comment involves the regulation of the cyclic AMP/cyclic GMP ratio by a balance between the rates of their synthesis and degradation by phosphodiesterases.

It is known that the two cyclic AMP phosphodiesterases from rat thymic lymphocytes exhibit different K_m values, 0.9×10^{-6} M and 8.0×10^{-6} M²⁶. The enzyme with the higher K_m is stimulated by cyclic GMP by increasing the V_{max} with no change in the K_m for cyclic AMP. Cyclic GMP competitively inhibits the enzyme with the lower K_m ²⁷. A partially purified preparation of phosphodiesterase from bovine heart had an apparent K_m value of around 2.0×10^{-6} M for cyclic GMP and more than 25×10^{-6} M for cyclic AMP. Both cyclic AMP and cyclic GMP interfered with the hydrolysis of each other in a manner predictable on the basis of their apparent K_m values. In liver extracts, cyclic GMP was found to stimulate hydrolysis of cyclic AMP²⁷. The finding that one cyclic nucleotide can alter the rate of hydrolysis of the other raises the possibility that the intracellular concentration of one cyclic nucleotide regulates the level of the other by influencing its rate of degradation. These studies provide a rationale as to why the two intracellular mediators of the inductive signal might be structurally related. Fine control of the ratio between them is possible, such that in one range it is buffered, and in another range it has a sharp rate of change. These considerations deal with the regulation of the ratio cyclic AMP/cyclic GMP but they leave open two questions. First, how is the ratio sensed by the antigen-sensitive cell? Second, in addition to reversing cyclic AMP inactivation, what is the pathway unique to induction that cyclic GMP triggers?

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LETTERS TO NATURE

PHYSICAL SCIENCES

Nature and Origin of Comets

In so many fields of astrophysics the textbooks and the ordinary review articles have a tendency to present only the 'generally accepted' point of view, often not mentioning alternative theories, and even sweeping under the rug those observational facts which are adverse to the dominant view. This also applies to the theory of comets. As the arrival of Comet Kohoutek, and also the space missions to comets which are now being planned, is focusing the interest on comets, we may have unique opportunities in the near future to clarify which views are correct. This calls for a survey of the controversial points. A partial list of these, with which we will be concerning ourselves here, is the following:

- (1) What is the physical nature of the cometary nucleus? (a) Does it invariably consist of a single monolith? or (b) could it, in some instances at least, constitute a bunch of particles having no physical coherence?
- (2) What is the genetic relationship between comets and the meteor streams with which they are associated? (a) Do the stream meteoroids invariably derive from the associated comets? or (b) is the reverse process also possible?
- (3) Is there a net dissipation or accretion during the lifetime of a comet?
- (4) What is the origin of short-period comets?
- (5) What is the origin of long-period comets?

Several other questions with regard to the chemical composition of the nucleus, the mechanisms for the production of the observed radicals and ions, and the nature of the comet solar-wind interaction merit discussion but are outside the scope of this letter.

The answers to all these questions are basically connected with the problem of how a swarm of particles in similar orbits will develop. There is a general belief that the collisions (and other types of interaction) between the particles will cause a diffusion so that a state according to Fig. 1a will develop to the state depicted in Fig. 1b. This is correct only under the assumption that the collisions are elastic (or have at least a minimum of elasticity). But a swarm of particles in periodic orbits whose collisions are inelastic will behave in the contrary way, passing from the state of Fig. 1b to the state of Fig. 1a. This is because inelastic collisions cause the orbital parameters to become more similar. Baxter and Thompson^{1,2} have treated the problem with the Boltzmann formalism and demonstrated that the 'diffusion coefficient' is negative. The same result may be produced if the particles in the swarm exchange momenta in other ways, such as by the particles emitting gas which in turn interact with other particles.

As we do not know the collisional properties of the meteoroids in space, it is impossible to decide whether the diffusion in a stream of particles is positive or negative. This cannot be clarified by the study of meteorites which have fallen on the Earth because their surface properties, which decide their collisional behaviour, have been drastically changed during their passage through the atmosphere. Furthermore these meteorites are a highly selected sample because only those meteoroids having high tensile strength and consequently high elasticity can survive the passage through the Earth's

atmosphere. Meteorites collected on the Moon's surface have impinged with at least the lunar escape velocity and have also been changed. From a study of them, Arrhenius and Asunma¹⁹ have put forward strong arguments for the view that space collisions are inelastic, so that the diffusion should be negative. Also luminosity and deceleration studies of stream meteoroids in the Earth's atmosphere lead to the conclusion that most of these have bulk densities well under 0.5 g cm^{-2} whereas in the case of the Giacobinids they may be as low as 0.01 g cm^{-3} (ref. 3), suggesting also low elasticities.

The first alternative of positive diffusion leads necessarily to the more generally accepted theory of the comet-meteor stream complex⁴. In this case the stream meteoroids which derive from a big solid chunk of ice and dust (Whipple's 'icy conglomerate') must diffuse both along and normal to the stream to be ultimately dispersed into interplanetary space (sporadic meteors).

According to the second alternative of negative diffusion a meteor stream can be kept together under the condition that the self-focusing effect exceeds the disruptive effects due to planetary perturbations and solar radiation (Poynting-Robertson effect and so on). As shown by Mendis⁵ this seems likely to occur under very general conditions. So a meteor stream may behave as a typical 'jet stream' discussed by Alfvén and Arrhenius⁶. Due to its very large accretion cross-section a meteor stream may also be able to collect a significant amount of interplanetary dust and gas⁵.

Further, Trulsen⁷ has shown that planetary perturbations of meteor streams, rather than producing a general disruption, may cause density waves which build up slowly. If several

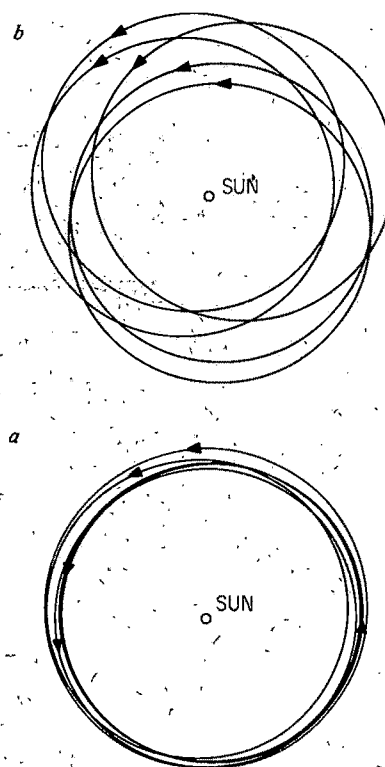


Fig. 1

such waves are progressing, very large density increases can be caused statistically at some points, leading to the formation of a dense cloud of particles. These in turn would ultimately agglomerate into a number of large chunks which may coalesce into one. This view then leads not to a single model of the cometary nucleus (as Whipple's 'icy conglomerate' or Lyttleton's 'sand bank') but rather is a whole hierarchy of models ranging all the way from a more or less loose agglomeration of small particles to a single monolithic nucleus, with the latter the most likely final stable state. Therefore although most comets possibly do have a single monolithic central nucleus, perhaps of the Whipple type, the possibility that there are comets with more than one nucleus or even consisting of a more or less loose swarm of grains cannot be ruled out. Indeed, the very dusty, gas deficient comets may belong to the latter type. There are several instances of observation of comets with multiple nuclei⁸⁻¹⁰. Whether these are the remnants of a single monolithic nucleus or merely the precursors of one is still an open question.

As regards the formation of comets in meteor streams there are several interesting observations which are suggestive of the latter process. For instance comet P/Temple-Tuttle ($P \approx 33.2$ yr) was first recorded as a diffuse but bright object only as recently as 1866 (ref. 11), although the associated Leonid meteor stream was known for centuries earlier. An even more significant observation concerns comet P/Swift-Tuttle ($P \approx 120$ yr) which was bright enough on its first apparition (in 1962) to be easily seen with the naked eye, being a 2 mag object at its brightest¹¹. What is surprising is its association with the Perseids meteor stream which has been observed for over twelve centuries¹².

There have been several claims by observers of actually having witnessed the formation of cometary nuclei⁹, but one hesitates to take these early observations at face value. More recently, however, Mrkos¹⁰ has stated that in the case of P/Honda-Mrkos-Pajdusakova no nucleus is seen when the heliocentric distance of the comet is > 0.7 AU even if it happens to be very close to the Earth (< 0.3 AU), while later on one begins to see not just one centre of light but several. Besides, this behaviour has been observed repeatedly. Interestingly, the comet probably also has an associated meteor stream (α -Capricornids).

We now turn to the question of the origin of long-period and short-period comets. The origin of the long-period comets is essentially unknown. The view that seems to be most generally held at the present time is that the long-period comets derived from the swarm of planetesimals out of which the outer 'icy' planets Uranus and Neptune (and perhaps to a lesser extent Saturn) formed. A small fraction of these planetesimals are believed to have been perturbed by the large planets into highly elongated orbits to form the long-period comets¹³. This view is basically not inconsistent with the planetesimal view of the formation of the Solar System (see, for example, Alfvén and Arrhenius (refs 6 and 14, and unpublished work), but long-period comets may still be forming as condensations in long-period meteor streams just as the short-period comets seem to do⁵.

As for the origin of short-period comets, the dominant view is that short-period comets derive from long-period comets that pass near one of the massive planets (especially Jupiter) and lose energy in the process. While single close encounters with Jupiter of the observed distribution of long-period comets are shown to be incapable of producing the observed distribution of short-period comets^{15,16}, Everhart¹⁷ has recently shown that the cumulative effect of many hundreds of passages near Jupiter of a low inclination belt of near-parabolic comets having initial perihelia near Jupiter's orbit could in fact produce such a distribution. It is, however, not clear at this stage if Everhart's calculations can resolve the crucial problem with regard to the origin of short-period comets, viz. the large observed number of these objects. P. C. Joss (unpublished) has shown on the basis of Oort's comet cloud

and the injection rate of new comets from this cloud into the inner Solar System that the above calculations fail by several orders of magnitude to explain the observed number of short-period comets. One can get around this difficulty, but only at the expense of introducing a new hypothesis, such as the existence of another distribution of long-period comets besides the observed one. This would be a disk distribution close to the ecliptic having dimensions $\lesssim 10^4$ AU and containing more than 10^9 comets⁵.

Everhart¹⁸ has recently shown that the observed distribution of short-period comets may also be derived by a process of diffusion from low inclination comet belts lying in between the major outer planets. There is, however, no evidence at the present time for any such belts.

But if one accepts that comets can be formed in meteor streams at the present time despite the competing disruptive processes, as has been shown by Trulsen⁷ and Mendis⁵, then this crucial difficulty with regard to the observed number of short-period comets is overcome. Meteor streams according to this view do not merely form a sink for short-period comets as is generally believed but also form a source, and a steady state may be maintained with the average rate of formation equalling the average rate of disruption⁵.

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Visual Determination of the Mean Effective Chromospheric Thickness

IN the course of taking submillimetre chromospheric data from Concorde 001 during the eclipse of June 30 (ref. 1), it proved possible to record information on the visual thickness of the chromosphere which is accurate enough to merit reporting. During an eclipse viewed conventionally from a stationary site on the ground, the precise time at which the solar photosphere reappears after totality, termed third contact, may be predicted to within 0.5 s (of time), given an adequate knowledge of the lunar limb topography, that is, to within 1 km in height at the appropriate point on the limb. Further, photometric measurements in white light could determine this time to within 0.3 s. It may also be possible

from the ground, under ideal observing conditions, to see and measure emission from the chromosphere which should be visible in isolation for around 3 s, just prior to third contact. The predominant radiation seen during this time is that of the first line of the Balmer series, $H\alpha$, at 6,563 Å which accounts for the traditional description of the phenomenon as the 'red flash'. It should be possible, after taking into account atmospheric scattering and diffraction effects, to measure the duration of this to within 0.5 s, though measurements of this type are not typically considered sufficiently accurate to be worth taking, when, for example, the flash spectrum of the chromosphere is also available². Although various observers^{3,4} have studied the chromosphere spectrally in emission during eclipse, both just after second contact and just before third contact, inaccuracies in our knowledge of the precise orientation of the Moon and its topography have made absolute heights above the photosphere very difficult to measure to better than 300 km, although relative heights may be estimated to within 100 km under ideal seeing conditions. Similar restrictions due to seeing apply to estimates based on $H\alpha$ filtergrams taken outside eclipse conditions⁵.

The apparent retardation of the eclipse by a factor of 15 when viewed from the moving aircraft provided a straightforward method of estimating the effective chromospheric thickness. With the eye entirely dark adapted after 74 min of totality, one could observe quite precisely a chromospheric third contact, followed 50 s later by photospheric third contact. As chromospheric third contact (CTC) occurred, the eye detected a sudden brightening at a point on the lunar limb which grew into a vivid red crescent. Through the 1-inch objective guider telescope for the main infrared experiment the crescent was seen to grow until it subtended an angle of some 40° at the disk centre, when a second step up in brightness occurred, and the colour changed at one point on the rim to the yellow of photospheric emission, thus marking photospheric third contact (PTC). This point too grew rapidly into a crescent, signalling that the aircraft had been overtaken by the edge of the umbra of the eclipse.

A fairly accurate estimate of the time interval between CTC and PTC was fortunately possible, as the observer was noting all observational changes verbally on a tape recorder. Subsequent timing showed that the estimate was subject to an error of up to 2.5 s at CTC and 0.5 s at PTC, the former error being due to a brief delay in recognising the phenomenon in unique circumstances. It is thus possible to state that the $H\alpha$ emission from the chromosphere was seen in isolation for 50 (± 3.0) s. The precise position of the plane for every second of time to within 1 km in terrestrial latitude and longitude, and the speed to 1 part in 10⁴ were provided by the navigator, M. Henri Perrier, using data from the inertia navigation system. With the aid of these data, and with the aid of subsequent computation by HM Nautical Almanac Office of the positions and standard semi-diameters of Sun and Moon seen from each point on the aircraft's trajectory, the observed time interval is convertible to an angular and then linear thickness of observed chromosphere. The apparent rate of passage of the Moon's limb across that of the Sun at both third contacts was 0.0795 arc s s⁻¹, while the linear scale for the Sun's disk was 1 arc s = 737.4 km. These conversion factors combine to yield a value for the chromospheric $H\alpha$ thickness of 2,900 (± 200) km above the photosphere at the time of the observation.

It is clear that this estimate does not imply any particular model for the chromosphere. No attempt could be made to deduce whether the radiation seen originates from a spherically symmetrical stratified layer or from inhomogeneities, in particular from spicules, known to be strong $H\alpha$ emitters, which cluster favourably in regions of enhanced magnetic fields along supergranular boundaries within the chromosphere⁶. There can be little doubt, however, in the light of other observations^{7,8} that spicules, which are optically thick in $H\alpha$ and the longest of which

extend in length to well over 10,000 km above the photosphere, could provide the bulk of the observed emission when viewed edge on in this way. It is estimated by Athay⁹ that, given the measured dimensions and properties of individual spicules as seen on the disk, their appearance seen edge on in $H\alpha$ light at eclipse would cease to be continuous at the height where they occupy 1% of the chromosphere surface area, above which individual spicules could be photographed separately. The present observations would set this 1% height close to 3,000 km above the photosphere. Further information on the distribution of spicules with height should become available when the sub-millimetre data, which were the ostensible objective of the experiment, have been fully reduced.

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Search for Atmospheric Gravity Waves induced by the Eclipse of June 30, 1973

Chimonas and Hines^{1,2} suggested that atmospheric gravity waves could be generated by the supersonic passage of the Moon's shadow through the Earth's atmosphere during a solar eclipse. Beer and May³ pointed out that the eclipse of June 30, 1973, would provide an opportunity of investigating the idea, and perhaps establish a link between travelling ionospheric disturbances (TIDs), as reported by other observers^{4,5}, and the eclipse phenomena. In addition, Beer and May predicted the positions of the hypothetical wavefronts for various times during and after the eclipse.

The gravity waves were predicted to have a period of 4 h and amplitude 10 μ bar at a position 10,000 km from the eclipse path¹. The TIDs reported around the times of previous eclipses had periods of the order of 20 min (refs 4 and 5). In an attempt to discriminate between the longer and shorter periods, a microbarograph was constructed with a variable pass band similar to that designed by Jones and Forbes⁶.

Our version of this instrument has a pass band determined

by two needle valves, which control slow and fast leaks to two otherwise identical metal bellows. The response function of this arrangement to sinusoidal variations in pressure is deducible theoretically, and for a typical configuration is shown in Fig. 1a. Pressure changes are measured by a plate which, attached to one of the bellows, forms part of a variable capacitor in a bridge network.

For calibration the whole instrument was placed in a sealed insulated pressure vessel, and the time constants τ_1 of the needle valves determined by maintaining one in a measured, almost closed position, while subjecting the instrument to a step-function pressure change; the measurement could then be repeated for a new set position. Figure 1b shows typical exponential outputs from which τ_1 are deduced, and Fig. 1c gives the experimental responses to sinusoidal pressure oscillations of different frequencies. Finally, an absolute amplitude calibration at zero frequency (that is, a static pressure response) was found.

On June 30 the instrument was set with a pass band of 30 to 7,000 s, giving a response of 145 μbar full scale deflection for waves with periods of 20 min. With such a low frequency cutoff, the instrument required fairly frequent readjustment to bring it back on scale. The trace for the period in which the gravity waves might have been expected was very 'noisy' due to the weather conditions. Figure 2a shows the trace from

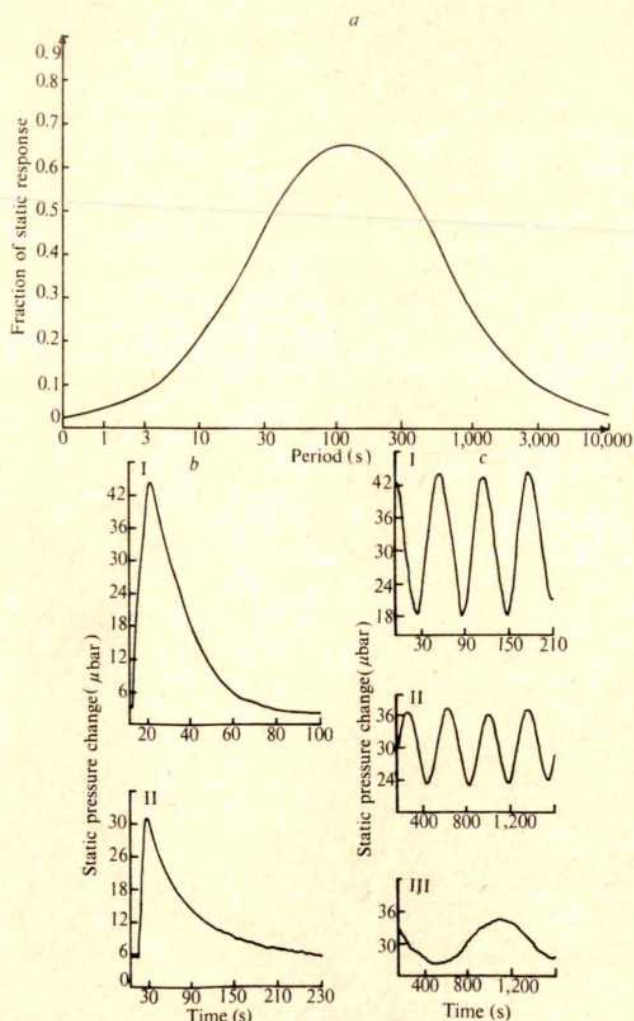


Fig. 1 a, Theoretical response curve for the microbarograph with fast leak set at 7 s and slow leak 80 s. b, Typical exponential outputs used to find τ_1 : I, valve setting 200° , chart speed 60 mm/M, τ_1 13.5 s; II, valve setting 240° , chart speed 20 mm/M, τ_1 80 s. c, Response of instrument to a sinusoidal pressure change of 30 μbar , but different periods: I, 63 s; II, 380 s; III, 1,140 s. Pass band (3 dB points on response curve) approximately 60 s to 300 s.

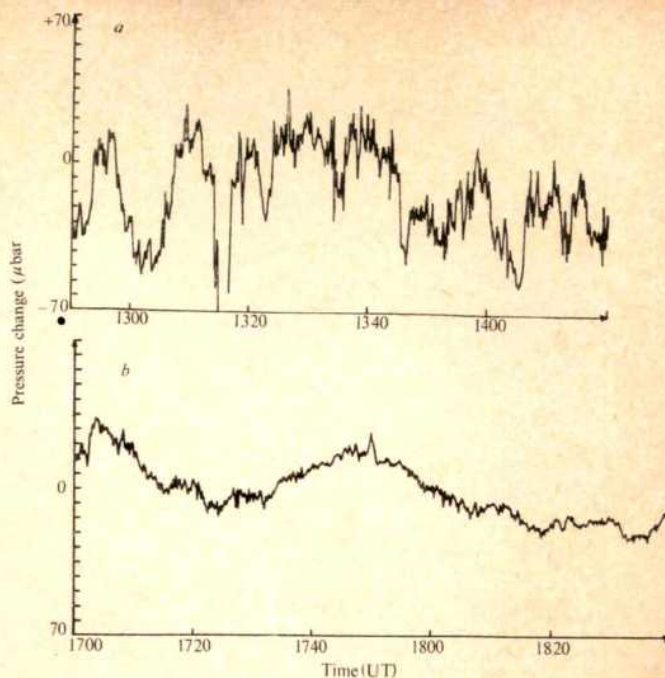


Fig. 2 a, Microbarograph record for the period 1250 UT to 1420 UT on June 30, 1973. b, Microbarograph trace in quieter conditions on a previous day. Sensitivity and pass band as for the observation on June 30.

1250 to 1420, and Fig. 2b illustrates a much quieter period on another day. There are two principal features on the trace; first, a sine wave starting at about 1257 UT with period 15 min and amplitude 60 μbar . It is possible that this is one of a train, though the earlier ones are smaller and difficult to make out in the noise. At 1314 UT a sharp decrease in pressure was recorded which sent the instrument off scale for about 2 min, after which the trace returned to its original noisy pattern.

These two features could just possibly be noise, but no other such isolated feature has been recorded during 50 d almost continuous operation. There were no meteorological fronts in the vicinity at the time of observation, and the duration was far too long to be the product of a sonic boom⁸.

Assuming great circle tracks and a speed of propagation of 320 m s⁻¹, the gravity wave should have reached the instrument after 1353 UT. It therefore seems that the most significant features recorded on the microbarograph could not be due to the eclipse. We have no evidence of any short period eclipse induced gravity waves, nor the long period waves predicted by Chimonas and Hines¹, though the instrument could not really be set up with a broad enough pass band to take in the lowest frequencies. It is hard to see how, in view of its timing, the isolated disturbance noted above could be connected with any effect of the eclipse, and we thus confirm the conclusion of Schödel, Klostermeyer and Röttger⁹.

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Rapid Variations Observed during the Total Eclipse of the Sun on June 30, 1973

FOR nearly a century the solar corona has been considered responsible for the interplanetary corpuscular radiation and in particular large streamers have been thought to be the main source of this radiation.

But during the past ten years many expansion models (solar wind) have been put forward; in these an important part is played by the hydrodynamical acceleration of the coronal plasma by solar gravity (gravitational nozzle). These models, however, always neglect one of the most important characteristics of the solar corona: that it is heterogeneous.

Information obtained during a total eclipse of the Sun (when the solar corona may be observed in critical regions where the specific acceleration of the plasma ($r \approx 3.5 R_{\odot}$) occurs) is naturally limited as the observation time was very short. During the total eclipses of July 10, 1972, and June 30, 1973, however, we attempted an experiment to observe the solar corona with the best spatial resolution possible at different moments separated by about 2 h. In fact the weather conditions were favourable during the most recent eclipse.

Two cameras, equipped with the same achromatic lenses $F=3,000$ mm and $\phi=200$ mm and the same compensators of brightness gradients (radial neutral filter), worked well—one in Mauritania near Atar, the other in Tchad near Moussoro. The total eclipse could be seen from these two observation points with a time difference of 1 h 30 min. Several plates were taken with the same instrumental para-

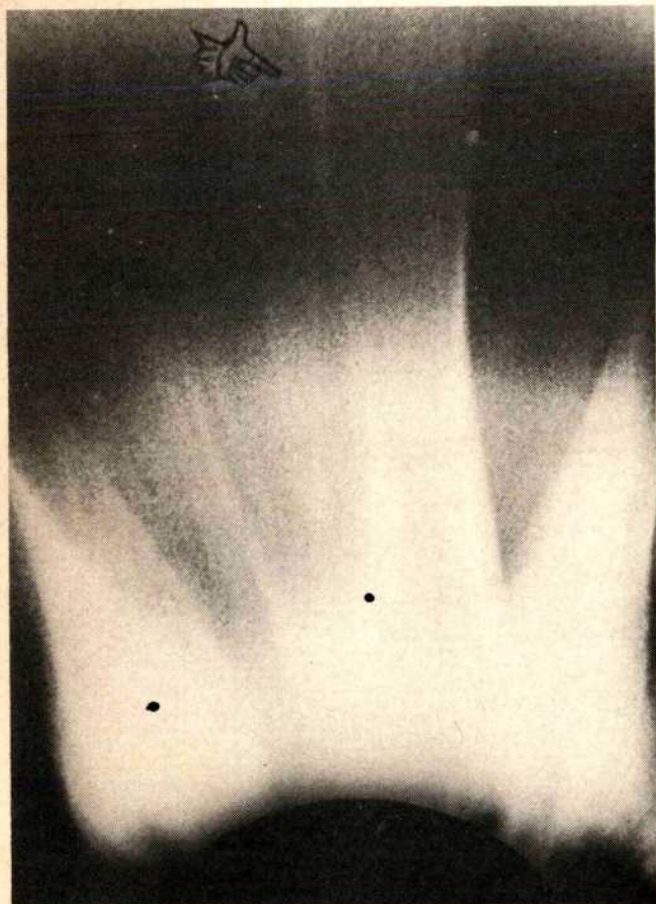


Fig. 1 Contrasted photograph of part of the plate taken at 1213 UT at Moussoro (Tchad) by the team of the Institut d'Astrophysique, Paris, showing the 'detachment' phenomenon of part of the large coronal streamer.

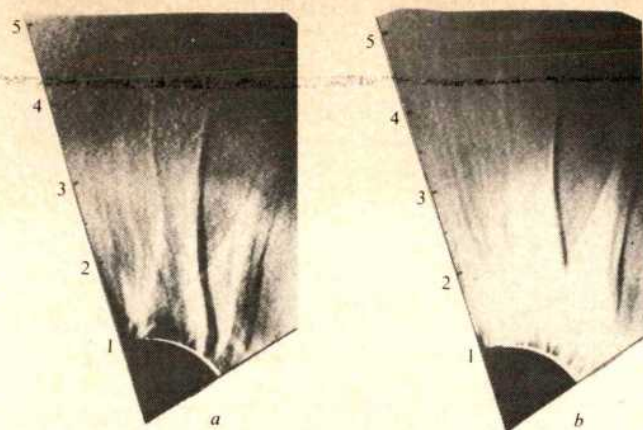


Fig. 2 A photograph made up of two plates taken with the same observational instruments at Atar, Mauritania, at 1046 UT (a, team from the University of Kiev, USSR) and at Moussoro at 1213 UT; (b, team from the Institut d'Astrophysique, CNRS, Paris). In order to increase the contrast in the outer regions the derivative of each photograph was obtained by compositing the negative and the positive copies together, shifted by $\Delta = 6 \times 10^{-2} R_{\odot}$ perpendicular to the streamer.

meters. Their detailed comparison will be the subject of future publications. In addition some weighted plates were obtained by a third group in Kenya with another instrument; its performance was not as good as that of our cameras ($F=1,550$ mm).

Most of the plates were made with Kodak films (18×24 cm); the exposure times were 10 and 20 s. Weather conditions were not excellent (on account of dust, nebulosity and so on). Nevertheless the exceptional length of the eclipse (maximum duration 7 min) enabled us to study the outer regions of the corona ($r \gtrsim 3 R_{\odot}$) with plates taken in the neighbourhood of the centre of the total eclipse, without being hindered too much by the sky background. We increased the nominal contrast ($\gamma \approx 1$) when developing the films so as to improve the resolution of the structural details. On all plates we managed to identify several stars of magnitude 6 and 7 which helped the comparison.

The plates obtained show many variations in structural details. A preliminary survey has nevertheless revealed a region situated in the outer corona ($r > 3 R_{\odot}$) to the west, where these variations have an exceptional characteristic (see Fig. 1). The end of the stalk of a large streamer seems to be a 'detachment' from the corona.

In fact in the region that we are considering, the plate obtained at 10.46 h clearly shows the end of the streamer—very thin and stretched out to $r \lesssim 3.85 R_{\odot}$ (radial distances are measured perpendicular to the line of sight). On the plate taken at 12.13 h, this part of the streamer has moved to a position which varies between 450,000 and 750,000 km ($r \lesssim 4.9 R_{\odot}$) according to the part of the streamer considered. It is then easy to calculate that the 'mean velocity' of the movement of the different parts of the streamer which are 'detached' varies from 90 to 140 km s⁻¹ according to their radial distances.

The information which has been gathered seems unique in the history of astronomy. This is not surprising, for observations with good spatial resolution (10") of the outer corona have only been made over very short periods of time. It is difficult, under such conditions, to evaluate correctly the frequency of the observed phenomenon. At least it would be reasonable to consider this phenomenon as typical of the evolution of the extremity of large coronal streamers. Probably the explanation is in terms of an instability phenomenon, linked with the behaviour of the streamer in the neighbourhood of the critical point ($r \approx 3.5 R_{\odot}$). We also note that this phenomenon seems to be connected with the evolution of a tangential discontinuity of the coronal plasma.

On the other hand, we do not exclude the possibility that the phenomenon of 'detachment' is connected with the propagation along the lines of force of the magnetic field of a perturbation which would have its origin in the chromosphere.

It seems difficult from these results to reconcile this description of the expansion phenomenon of the outer solar corona with the hypothesis, accepted up till now, of quasi-stationarity at least in the ranges considered here, which are of the order of 10^5 km.

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Possibility of Determining Intergalactic Gas Density by Radio Observations of Flares of Remote Sources

DETERMINATION of the mean gas concentration in intergalactic space (N_{mg}) is an important problem which is still far from being solved. One may hope finally to determine the value of N_{mg} in different indirect ways (see, for example, ref. 1). At the same time there is a possibility of finding N_{mg} directly by measuring the radio signal retardation time $\tau(v) = t(v) - t(\infty)$ for a frequency v , where $t(\infty)$ is the time of the arrival of a signal of a rather high frequency. In a completely ionized gas the refractive index $n = 1 - (e^2 N / 2\pi m v^2)$, the group velocity $u = cn$ and

$$\tau(v) = L/u - L/c = e^2 N_{\text{mg}} L / 2\pi m c v^2 = 1.34 \times 10^{-3} (N_{\text{mg}} L / v^2) \text{ s}$$

where L is the distance to the signal source assuming $(1 - n) \ll 1$; the accuracy of the expressions used is clear (for example, from ref. 2). For our Galaxy, at not very small galactic latitudes, $\int N_{\text{g}} dl \equiv N_{\text{g}} L_{\text{g}} \sim (10^{20} \text{ to } 10^{21}) \text{ cm}^{-2}$. Therefore at $N_{\text{mg}} \sim 10^{-5} \text{ cm}^{-3}$ the product $N_{\text{mg}} L > N_{\text{g}} L_{\text{g}}$ if $L > 10^{25} \text{ to } 10^{26} \text{ cm}$. Thus, for extragalactic sources at more than 3 to 30 Mpc signal retardation in intergalactic space at $N \gtrsim 10^{-5}$ is greater than in the Galaxy and could be measured (I note, as an example, that at $N \sim 10^{-5}$, $v \sim 3 \times 10^7 \text{ Hz}$ and $L \sim 10^{25}$, the time $\tau \sim 100 \text{ s}$). To apply this method, which is widely used in the case of pulsars³, there must, however, exist rapidly varying and powerful extragalactic radio emission sources; these have not yet been found.

I wish to draw attention to the possible appearance of suitable signals produced in the flares of supernovae or some other sources. I have in mind not entirely hypothetical considerations, which have already been widely discussed, but events connected with the cosmic γ -ray flashes recently discovered^{4,5}. (N. S. Kardashov mentioned (personal communication) that the possibility of observing radio emission correlated with the appearance of 'optical' supernovae in other galaxies has already been discussed. But, both by the conditions of usual optical observations and by the very nature of the γ bursts observed, they do not correlate with optical supernovae (see

also ref. 4) but do correlate with the radio bursts discussed here. Nevertheless, supernovae or unusual supernovae may be the sources of the γ bursts under discussion.) These flashes (with characteristic duration of the order of 0.1 to 10 s) are possibly caused by supernovae flares (at the initial stage of their evolution) at 1 to 10 Mpc (in the near future such events will be evidently observable also up to distances of 100 Mpc (ref. 5)). If such an explanation⁴⁻⁶ is correct, then in a flare an energy $W \sim 10^{47} \text{ to } 10^{48} \text{ erg}$ is transferred to γ rays and at least this energy is likely to be contained in the upper envelope of the star expanding at velocity $v \sim c$. In the course of further expansion this envelope must radiate mainly longer waves and particularly radio emission. The most effective processes are probably magnetobremstrahlung (some magnetic field is certainly present inside the envelope) and different collective (plasma) mechanisms of radio emission.

It is hardly possible to estimate reliably the power or the total energy of radio emission. I do not see, however, any reason to deny the possibility of an energy output in a radio band of, say, $W_r \sim 10^{-6} \text{ to } 10^{41} \text{ to } 10^{42} \text{ erg}$. For a distance $L \sim 30 \text{ Mpc}$ this corresponds to the density $S = W_r / 4\pi L^2 \sim 10^{-12} \text{ to } 10^{-11} \text{ erg cm}^{-2}$ or for a band $\Delta v \sim 10^9$ it corresponds to the spectral density $10^{-21} \text{ to } 10^{-20} \text{ erg cm}^{-2} \text{ Hz}^{-1}$. These figures are, of course, arbitrary but help us to realise that in the region 30 to 300 MHz, particularly interesting for measurement of $\tau(v)$, the radio emission flux may be sufficient for detection. It seems reasonable to use several points of observation (see refs 7 and 8) and, of course, with correlation of radio measurements with γ measurements on satellites. The possibility is not excluded that it would be possible to register γ bursts even on the Earth's surface by observing some perturbations in the upper atmosphere induced by these bursts (primarily, I have in mind optical flashes arising at a considerable part of the Earth). Radio flashes should evidently retard by comparison with γ flashes (both on account of the influence of plasma during propagation and on account of the generation conditions), and radio signals of lower carrier frequency (according to the conditions of propagation and probably also to those of generation) should retard by comparison with signals of higher carrier frequency. If radio signals seem to be polarised, measurement of the polarisation parameters at different frequencies will yield additional information and first of all the mean value of $N(H)$ along the line of sight. (Here H is the projection of the magnetic field at the direction of observation.) Since the connection of the observed γ events with supernova flares is not yet proved, I note that the appearance of radio flashes is also probable for some other possible sources and will help to clarify their nature (for example, if these sources are galactic, that is, they are some flaring stars, the retardation $\tau(v)$ may prove insignificant).

Although the appearance of the type of sufficiently powerful radio signals discussed cannot be guaranteed, the corresponding observations seem fully justified.

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BIOLOGICAL SCIENCES

Distribution of Microorganisms in Hailstones

LARGE numbers of microorganisms are present in the residues of hailstones, together with other insoluble particles. As the hailstone is the surviving testimony of the life history of a storm and as the organic material can be considered a natural 'tracer' of the ingested air mass, it is natural to investigate whether any information about the conditions in which hailstones grow can be deduced from the internal distribution of microorganisms.

Cloud physicists are in fact in search of new parameters with which to determine the growth conditions in the cloud solely from an examination of the hailstones collected. Aerobiologists, on the other hand, are interested in the aerosolisation, diffusion in the atmosphere, transport and removal of aerospora; in this cycle the process of in-cloud scavenging and washout by precipitation elements plays an important role for particles of low fall velocity ($\sim 0.3 \text{ cm s}^{-1}$ for a $10 \mu\text{m}$ particle of density 1 g cm^{-3}). Thus there are two good reasons for investigating the presence of microorganisms in precipitations. Surprisingly, however, the subject remained almost unstudied in detail even though it was discovered a long time ago¹.

As former work dealt with the melting of complete hailstones² our interest centred on the local distribution of germinating microorganisms inside hailstones relative to the internal features. Non-germinating particles (pollen and fungal spores) have also been identified and counted with a microscope. We chose for the test a giant ellipsoidal hailstone, largest dimension about 7 cm, which was collected during the summer of 1969 near Garden City, Kansas.

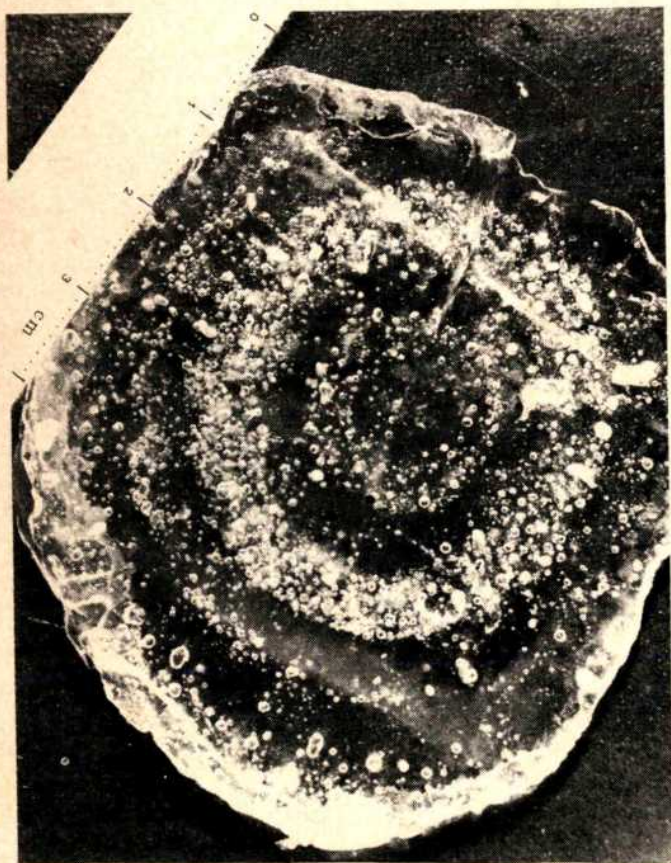


Fig. 1 Hailstone slice, as seen in reflected light, showing the sequence of opaque-bubbly and transparent layers.

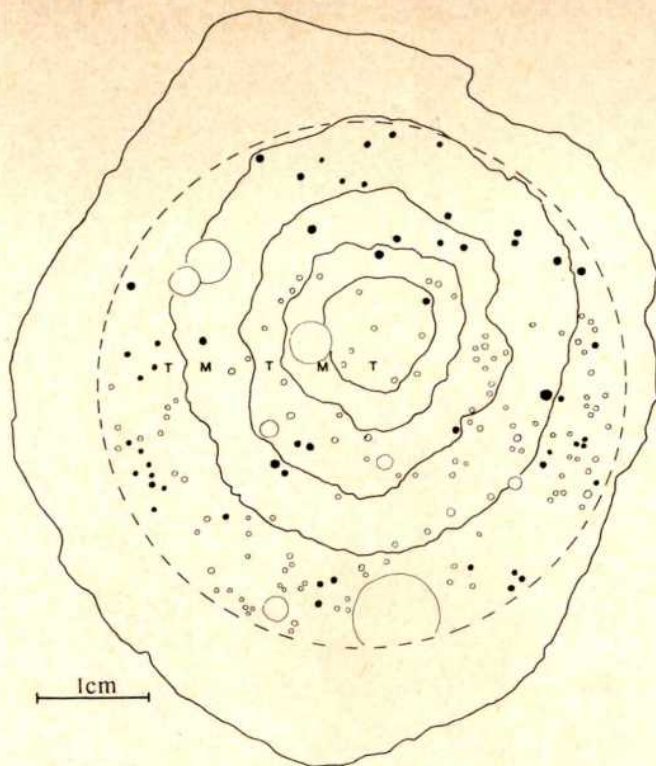


Fig. 2 Distribution of bacterial and fungal colonies grown on the concentric series of filters; the black disks represent colonies grown 24 h later than those represented by empty circles. The map has been superimposed on the outlines drawn from Fig. 1 and shows layers of opaque (M) and transparent (T) ice. The hatched circumference defines the area that has been examined.

A slice 2 mm thick was sawn off the main section and prepared with a microtome. All operations, including working, melting and filter preparation, were carried out in sterile conditions. The slice was then photographed in crossed polaroids and reflected light. The external layer was washed with sterile water to eliminate possible contamination and the slice was placed on a concentric array of membrane filters (pore size $0.45 \mu\text{m}$) of different diameters in a sterilised filter holder (diameter 142 mm) connected to a vacuum pump.

The particles deposited on the filters maintained their original locations on account of the very slow melting of the bottom of the slice. The filters were then separated and placed in different Petri dishes containing a nutritive medium³ and incubated at 24°C . Other slices of the same hailstone were melted and filtered, and the residues observed with the microscope. The results are shown in Figs 1 to 3. Figure 1 is a photograph of the slice in reflected light, which indicates the alternating sequence of opaque-bubbly and transparent layers. A map of the colony distribution has been superimposed (Fig. 2) on the outline of the internal features of the hailstone as deduced from Fig. 1. A graph of the radial distribution of micro-organism concentration for the different layers of the stone is shown in Fig. 3. There is a general decrease in the concentration of colonies towards the centre of the slice. More surprising, however, is the remarkable correspondence with the internal features: in the opaque layers there is only one-third to one-half of the colonies found in the transparent layers.

The increase with radius of the number of germinating colonies is in agreement with the results of Rosinski⁴ for giant aerosol particles in different hailstones. Possible explanations of this result are in terms of the increase of

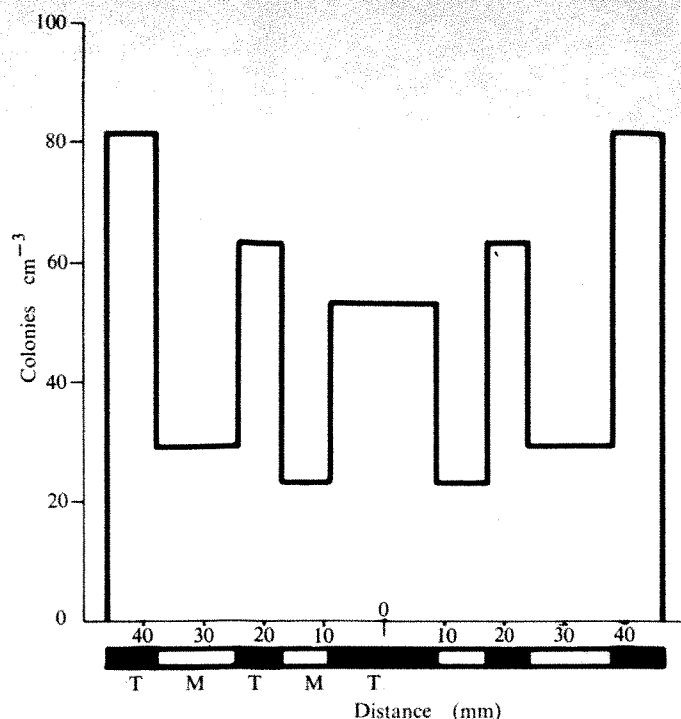


Fig. 3 Histogram of the distribution of colonies grown on the areas M and T represented in Fig. 2.

particle concentration in the accreting droplets and the intense evaporation of the hailstone, which is much warmer than its environment during the final stage of growth. It seems more difficult, however, to interpret the correspondence of the colony concentration with the sequence of layers. The lower density of the opaque-bubbly layers cannot alone explain the lower content of colonies. In fact measurements of local density in hailstones⁵ show, for this type of hailstone, a maximum reduction of 10% in density due to the presence of air bubbles. On the other hand, the high collision efficiency of large cloud droplets for particles of the size of airborne microorganisms suggests that organic material is transferred to the hailstone more through capture of droplets than through direct aerodynamic capture. If so, the opaque layer and the lower particle content would both have been consequences of accretion with a narrower spectrum of cloud droplets. The possibility that the variations in particle concentration are due to variation in the evaporation rate during the hailstone growth cannot, however, be excluded. Rejection of particles by the advancing ice-water interface during the final freezing is important only in very spongy growth, which is not the case for the hailstone examined.

It seems, however, that a necessary feature of further investigations will be the measurement of the aerospora profile in the environmental air together with knowledge of the circulation pattern of the storm, especially concerning the updraft levels.

As far as the identification of germinated colonies is concerned, only 3% are fungi (two colonies of Ascomycetes, one of which is a *Penicillium* sp., and three colonies of Moniliales, one of which is a *Cladosporium* sp.); the remainder is made up of a single type of Gram-positive streptococcus.

The aerospora composition seen only at the microscope of other slices from the same hailstone is quite different: *Alternaria*, 30%; *Cladosporium*, 9%; *Torula*, 1%; other Dematiaceous fungi, 26%; basidiospores, 4%; other spores, 23%; *Pinus* pollen, 5%; and other pollen grains, 2%. The concentration of the total aerospora is four times that of the

germinating colonies. Apart from mortality due to stress inside the hailstorm, some of these organisms could have been damaged during long storage in the freezer, including the air travel to Europe in a dry-ice container. This is confirmed by the observation that the incubation time before germination was longer for this than for other 'fresh' hailstones (4 to 5 d instead of 1 to 2 d).

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Phagocytic Release and Activation of Human Leukocyte Procollagenase

DESTRUCTION of collagen-containing structures occurs in those inflammatory disease states which are characterised by the infiltration of large numbers of granulocytic leukocytes¹. The degradation of collagen fibrils is probably mediated by a specific mammalian collagenase, since native collagen at physiological pH and temperature is resistant to hydrolysis by other proteolytic enzymes². Active collagenase initially identified in culture fluids of tadpole tail³ has since been demonstrated in cultures of human skin⁴, gingiva⁵, and rheumatoid synovium⁶. Furthermore, collagenase has been demonstrated in human rheumatoid synovial fluid and extracted directly from human granulocytic leukocytes^{7,8}. Recently, an inactive collagenase precursor was extracted from human leukocytes⁹. We now report that a collagenase precursor is liberated in large quantity from viable cells during phagocytosis of aggregated human γ globulin (AHGG). In addition, we show that the neutrophil is the principal source of this proenzyme, with only small amounts present in lymphocytes or lymphoblasts. The proenzyme can be activated by trypsin or rheumatoid synovial fluids but not by osteoarthritic synovial fluid.

Human leukocytes were isolated by dextran sedimentation of peripheral blood obtained from healthy volunteers negative for rheumatoid factor. The leukocyte-enriched fraction consisted on the average of 50% neutrophils, 42% lymphocytes, 6% monocytes and 1-2% eosinophils. A neutrophil-free population of mononuclear cells (95% lymphocytes, 5% monocytes) was isolated by isopycnic sedimentation in Ficoll-hypaque¹⁰. The purified mononuclear cell population was either used immediately or cultured in Medium 199 with HEPES buffer containing 15% foetal calf serum, penicillin, streptomycin and 20 μ l ml⁻¹ of phytohaemagglutinin-P (PHA-P) for 3 d at 37° C. Transformation to large lymphoblasts by PHA was monitored by incorporation of ³H-thymidine. Cell lysates (mixed leukocytes, lymphocytes or PHA-transformed lymphocytes) were prepared by suspending each of the various cell populations in Hanks' balanced salt solution (BSS) containing 1% glucose. The suspensions were frozen and thawed ten times and homogenised in a Dounce homogeniser. The resultant homogenates were dialysed, lyophilised and stored at -70° C for as long as 1 week. The lysates were reconstituted with distilled H₂O

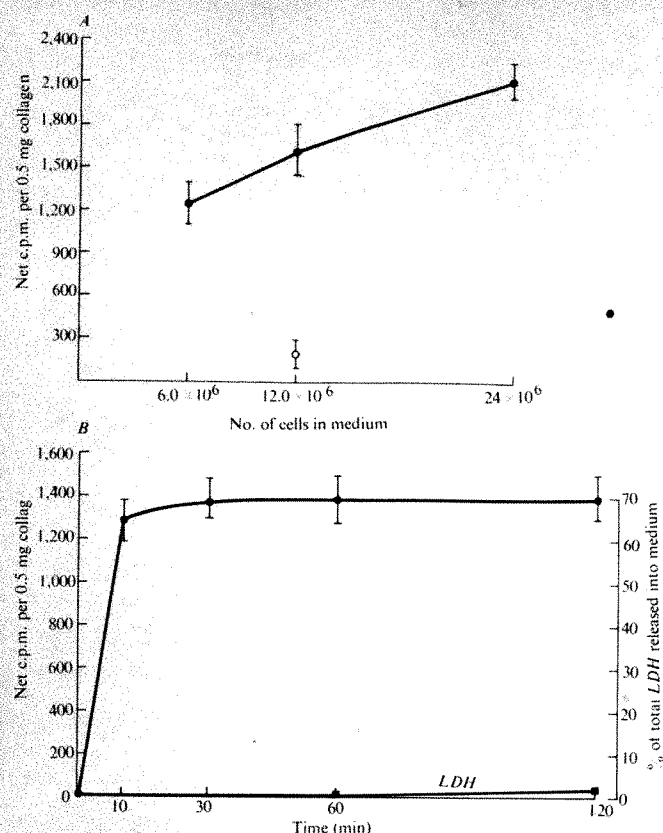


Fig. 1 *A*, Release of procollagenase from mixed leukocytes during phagocytosis of aggregated human IgG (AHGG). Supernatants were activated by exposure to rheumatoid synovial fluid as detailed in text. ●, Cells incubated with AHGG. ○, Cells incubated with buffer only (no AHGG). Each point represents mean $\pm$ s.e. *B*, Effect of incubation time on the release of procollagenase from mixed leukocytes during phagocytosis of AHGG. Supernatants were activated by $30 \mu\text{g ml}^{-1}$ of trypsin and the reaction terminated with 10^{-3} M TLCK. ●, Mean collagenolytic activity $\pm$ s.e. after trypsin. ■, Percentage of total LDH released into medium.

and centrifuged at $25,000g$ for 15 min before assay for collagenolytic activity or activation. In experiments involving phagocytosis, triplicate samples of 5 – 25×10^6 leukocytes were suspended in Hanks' BSS with 1% glucose (pH 7.5) containing 2% AHGG¹¹. Following incubation for 1–2 h at 37°C , an aliquot of the supernatant was utilised for estimation of lactic dehydrogenase (LDH) activity¹² and the remainder was dialysed against water at 4°C for 24 h, lyophilised and reconstituted when needed in 0.1 M Tris buffer. Whole cell lysates or the supernatant from phagocytosis experiments were activated by exposure at $30.0 \mu\text{g ml}^{-1}$ of TPCK trypsin (Sigma) for 1 h at 25°C . The trypsin reaction was terminated by addition of 10^{-3} M N- α -*p*-tosyl-L-lysine chloromethyl ketone (TLCK, Sigma). In other experiments whole cell lysates of phagocytosis supernatants (400 μl) were mixed with 25 μl of osteoarthritic or rheumatoid arthritic synovial fluids (obtained by knee puncture and supplied by Dr M. Ziff, Southwestern Medical School).

^{14}C -Labelled native neutral salt-soluble collagen was prepared by the method of Kang *et al.*¹³. Before use ^{14}C -collagen was reconstituted as a 0.2% gel according to the method of Gross¹⁴. The labelled collagen had a specific activity of 6,400 c.p.m. mg^{-1} collagen. To assay for collagenolytic activity, an aliquot of the sample was added to 250 μl of a 0.2% collagen gel (containing 0.5 mg collagen) to which had been added 200 μl of Tris- CaCl_2 , pH 7.4. After incubation for 18 h at 37°C , the reaction was terminated with 10^{-2} M EDTA and the mixture centrifuged at $15,000g$ for 30 min. A 0.5 ml aliquot was added to 10 ml of scintillation fluid (Insta-gel, Packard) and analysed for ^{14}C activity. In addition

to appropriate buffer blanks, all experiments included $35 \mu\text{g ml}^{-1}$ of trypsin to quantify the extent of non-specific gel breakdown. An Ostwald viscometer with a flow time for water of about 95 s at 22°C was used for relative viscosity measurements. Rheumatoid-fluid-activated procollagenase (obtained from 10×10^6 cells during phagocytosis of AHGG) caused a 30–35% decrease in viscosity during 24 h of incubation.

Table 1 Presence of Procollagenase in Human Leukocytes and its Activation by either Rheumatoid Synovial Fluid or Trypsin

Type of cell lysate	Activator	Collagenase activity net c.p.m.
—	Trypsin ($35 \mu\text{g ml}^{-1}$)	484 ± 25
—	Trypsin ($35 \mu\text{g ml}^{-1}$) + 10^{-3} M TLCK	65 ± 8
Leukocytes * (15×10^6)	None	98 ± 15
Leukocytes (5×10^6)	Trypsin ($30 \mu\text{g ml}^{-1}$)	667 ± 80
Leukocytes (10×10^6)	Trypsin ($30 \mu\text{g ml}^{-1}$)	$1,450 \pm 120$
Leukocytes (15×10^6)	Trypsin ($30 \mu\text{g ml}^{-1}$)	$2,007 \pm 150$
Lymphocytes † (5×10^6)	None	0
Lymphoblasts-PHA (5×10^6)	None	55 ± 5
Lymphocytes (15×10^6)	Trypsin ($30 \mu\text{g ml}^{-1}$)	670 ± 10
Lymphoblasts-PHA ‡ (15×10^6)	Trypsin ($30 \mu\text{g ml}^{-1}$)	650 ± 20
—	Osteoarthritic fluid	168
—	Rheumatoid fluid	145
Leukocytes (30×10^6)	Rheumatoid fluid	2,827
Leukocytes (30×10^6)	Osteoarthritic fluid	113
Bacterial collagenase ($10 \mu\text{g ml}^{-1}$)	—	$3,209 \pm 50$
Bacterial collagenase ($0.1 \mu\text{g ml}^{-1}$)	—	$2,944 \pm 25$

The buffer blank of 250 c.p.m. was subtracted from all samples.

* Mixed leukocyte suspension consisted of 50% neutrophils, 42% lymphocytes, 6% monocytes and 1–2% eosinophils.

† Lymphocyte population was free of neutrophils and consisted of 95% lymphocytes and 5% monocytes.

‡ PHA transformation of lymphocytes was monitored by ^3H -thymidine incorporation. PHA-transformed cells contained 15,000–20,000 c.p.m. per 5×10^6 cells, while normal lymphocytes did not incorporate significant amounts of ^3H -thymidine.

Control ^{14}C -labelled collagen gels incubated for 18 h at 37°C released about 250 c.p.m. (Table 1) and incubation with $35.0 \mu\text{g ml}^{-1}$ of trypsin caused the additional release of 484 c.p.m. The addition of 10^{-3} M TLCK almost totally inhibited the release of ^{14}C -peptides by trypsin. In another experiment a solution of $40.0 \mu\text{g ml}^{-1}$ of trypsin and 10^{-3} M TLCK had no detectable proteolytic activity when assayed against a 0.1% solution of azacoll for 40 min at 37°C . There was a linear increase in ^{14}C release from the gels when the trypsin-activated lysates from 5, 10, or 15×10^6 leukocytes were used. Lysates of normal lymphocytes, or PHA-stimulated lymphocytes, did not induce significant ^{14}C release. In the presence of trypsin the lysate of 15×10^6 lymphocytes or lymphoblasts solubilised about 20% of the ^{14}C -collagen gel which is equivalent to the release observed with 5×10^6 mixed leukocytes. Since the lymphocytes were a pure population and the leukocytes were composed of about equal numbers of granulocytes and mononuclear cells, it is apparent that the granulocytes contained approximately six times more proenzyme than did the lymphocytes.

Various arthritic synovial fluids were incubated with lysates from 30×10^6 leukocytes. Rheumatoid fluid used alone released 145 c.p.m., but when mixed with non-trypsin-treated leukocyte lysates 2,827 c.p.m. were released (Table 1). Osteoarthritic fluid did not activate the lysate procollagenase. A repeat of the experiment using two different arthritic fluids produced essentially the same results. Solutions of 0.1– $10.0 \mu\text{g ml}^{-1}$ of purified bacterial collagenase (Worthington) solubilised 78%–100% of the gel within 18 h (Table 1).

To determine whether human leukocytes could release

procollagenase during the process of phagocytosis, intact cells (triplicate determinations) were incubated with AHGG for 2 h at 37° C. Aliquots of the supernatants were removed, incubated with rheumatoid arthritic synovial fluid and the mixture was added to ¹⁴C-labelled collagen gels. There was a direct relationship between the number of cells in the medium and collagenolytic activity (Fig. 1A). The supernatant from 12 × 10⁶ cells incubated with buffer (no AHGG) and then with rheumatoid joint fluid was inactive. To estimate the rate of proenzyme release, a constant number of cells (6 × 10⁶) was incubated in triplicate with 2% AHGG for 10, 30, 60 and 120 min at 37° C. The supernatants from these experiments were activated with trypsin and the reaction terminated with 10⁻³ M TLCK. Maximum proenzyme release occurred within 15 min of exposure of intact leukocytes to AHGG (Fig. 1B). An estimation of cell viability during phagocytosis was obtained by assaying the supernatant for LDH activity. Less than 3% of the total LDH from 6 × 10⁶ leukocytes was released into the medium during the 2 h incubation (Fig. 1B), and in addition >95% of these cells excluded trypan blue dye.

A collagenase precursor has recently been demonstrated in organ cultures of tadpole tail¹⁵, mouse long bone and in human leukocytes. In mouse bone, procollagenase has been shown to be activated by limited proteolysis with trypsin, chymotrypsin or purified lysosomes¹⁶. Human leukocyte procollagenase activation was achieved by rheumatoid synovial fluid⁹. We now confirm these studies since lysates of human leukocytes were activated by either trypsin or rheumatoid synovial fluid but not by osteoarthritic fluid. In addition, we show that the neutrophil contains the highest content of the proenzyme, while the normal or PHA-transformed human lymphocytes contain approximately one-sixth as much. The collagenase precursor was released from viable human granulocytes in relatively large quantities under physiological conditions during the process of phagocytosis of AHGG. The phagocytic release of various other enzymatically active proteases from human leukocytes including β -glucuronidase, elastase and neutral protease has been demonstrated^{11,17,18}. There is, however, a significant difference in the kinetics of the release of the procollagenase since maximum lysosomal enzyme release (neutral protease) occurs in 90–120 min¹¹, whereas the procollagenase is probably released in the form of a brief pulse (within 15 min). The fact that the rate of procollagenase release differs so markedly from other granule-bound enzymes suggests that the proenzyme may be localised in a different subcellular fraction.

The pannus of the rheumatoid joint has the ability to produce an active collagenase and invade and degrade cartilage *in vitro*¹⁹. This implies that collagenase may be a significant factor in the pathology of rheumatoid arthritis. The demonstration of a collagenase precursor released during phagocytosis of aggregated human IgG and activated by a proteolytic enzyme or rheumatoid arthritic synovial fluid may also contribute to the joint degeneration seen in rheumatoid arthritis, a disease characterised by a large immigration of leukocytes to the inflamed joint. Leukocytes have been shown to phagocytose immune complexes present in the rheumatoid joint²⁰. The *in vivo* release of procollagenase during phagocytosis and its subsequent activation by the rheumatoid synovial fluid could then give rise to active collagenase which could result in the initial split in the collagen molecules of joint cartilage²¹. The neutral protease, which we have already shown is released by the leukocyte during phagocytosis¹¹, would then complete the degradation of the collagen fibrils of joint cartilage. In addition, Harris has shown that human leukocyte collagenase can destroy cartilage collagen, although the rate of degradation is slower when compared to its effect on native reconstituted skin collagen fibrils²².

The failure of osteoarthritic fluid to activate human leuko-

cyte procollagenase is consistent with the hypothesis that osteoarthritic joint destruction may be mediated by physical trauma rather than enzymatic destruction.

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Detection in Normal Plasma of Immunoglobulin resembling the Protein of γ -Chain Disease

TUMOURS of the lymphoid system have from time to time presented protein products apparently unique to the neoplastic process, but found later to occur in inconspicuous amounts in the normal organism. Thus Bence Jones protein was described in the urine of a patient with multiple myeloma in 1848 (ref. 1), found in about 10⁻⁴ times this amount in normal urine 112 yr later², and soon after recognised in both the pathological and normal circumstances to consist of free immunoglobulin light chains^{3,4}. More recent discoveries of undescribed myeloma proteins are apt to be followed rapidly by recognition of their normal analogues⁵⁻⁷. No normal analogue of the protein of the type described in 1963 by Franklin *et al.* in association with a disseminated lymphoid tumour^{8,9} has, however, been described. The tumour was called 'heavy chain disease' because it was seen to be secreting⁹⁻¹¹ an unusual protein related to immunoglobulin heavy chains. Heavy chain disease is now divided into three types¹²: according to whether the associated protein is related to the γ , α or μ class of heavy chains the disease is called γ , α or μ chain disease. The original case was of γ chain disease, and up to August 1972 thirty such cases had been recorded¹².

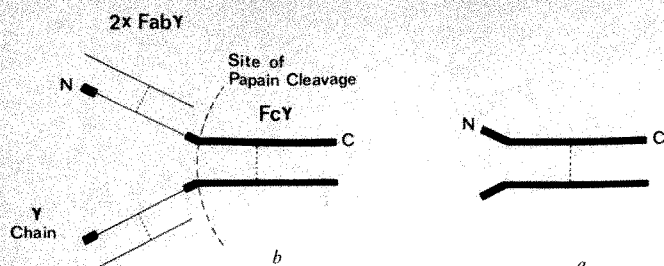


Fig. 1 *a*, The structure found for homogeneous γ CD proteins; *b*, that of human IgG. IgG consists of two γ chains and two light chains, joined by interchain bonds . . . , and cleaved by papain into one FcY and two FabY fragments as depicted. The heavy lines show the sequences represented in γ CD proteins. These have a small N-terminal sequence typical of whole γ chain, then after an apparent deletion of 100–200 amino acid residues a stretch of more than 200 residues embracing the entire C-terminal half; that is, the FcY region. The antigenic structure of γ CD proteins, deriving from the bulk of their sequences, resembles that of FcY.

Studies^{13–15} of a well characterised γ -chain disease (γ CD) protein revealed an N-terminal sequence of eighteen amino acid residues typical of whole γ chains, but a sequence from residue 19 to the C terminus identical with a γ -chain sequence from residue 216 to the C terminus: thus it looked like a γ chain with an internal deletion of 198 residues (Fig. 1). As appears likely from Fig. 1 the γ CD protein had all the FcY antigenic determinants but insufficient FabY sequence to give any FabY determinants.

Other γ CD proteins were soon found with similar but not identical internal deletions. They appear to fall into two groups^{15,16}: one of proteins themselves homogeneous, but with internal deletions varying from one to another; the other of proteins with heterogeneous N-terminal sequences, perhaps resulting from some postsynthetic degradation of proteins resembling those of the first group. The internal deletion has been much discussed with regard to its implications for the molecular genetics of immunoglobulins^{17,18}.

We have sought and found in normal human plasma a protein resembling γ CD protein by three criteria. First, a molecular weight appreciably less than that of IgG (150,000); second, an antigenic structure containing FcY but not FabY determinants; third, N-terminal peptides containing the cyclised residue pyrrolidonecarboxylic acid (PCA), typical of whole γ chains. A preparative procedure was designed to yield only protein satisfying the first two criteria ('FcY-like' protein), and this was then analysed for N-terminal PCA.

Figure 2 illustrates the preparative procedure. Precipitin analysis by the Ouchterlony technique revealed that the isolated FcY-related protein consisted of at least two components. One (FcY-like) contained only FcY determinants. The other ('IgG-like') had both FcY and FabY determinants. The IgG-like protein was removed by passage through Sepharose 4B-(rabbit anti-human FabY), and awaits further characterisation.

Upon analytical centrifugation the FcY-like protein sedimented as a single symmetrical peak, with $S_{20} = 3.9S$ in Tris-NaCl. Ouchterlony analysis with anti-FcY serum revealed a reaction of antigenic identity with authentic FcY; there was no reaction with anti-FabY nor with anti-(light chain) sera. Immunoelectrophoresis with the anti-FcY serum revealed a single broad arc of precipitation in the β - γ mobility region.

The protein was examined for N-terminal PCA by a method adapted from Press, Piggot and Porter²¹. A sample of 11.5 mg was fully reduced and alkylated, and digested for 3 h at 37° C with Pronase at pH 8.1 and an enzyme:

substrate ratio of 1:25 (w/w). The digest was run through a column of Dowex 50 (X2, H⁺ form). Unbound material was eluted with water and concentrated by desiccation under reduced pressure. When spotted onto Whatman 3 MM paper it gave a negative ninhydrin reaction and a strongly positive reaction with the hypochlorite/starch-iodide reagent of Rydon and Smith²². When tested by high voltage electrophoresis at pH 6.5 on thin-layer silica gel plates it resolved into three acidic and one very faint neutral spot, all stained by hypochlorite/starch-iodide (Fig. 3).

The presence after these procedures of acidic material staining with starch-iodide and not with ninhydrin has been unique to proteins having N-terminal PCA^{21–24}. Comparison of the mobilities of the spots with those of standard PCA and PCA-containing peptides (Fig. 3) suggests further that the FcY-like protein has yielded PCA, PCA-Val and PCA-Val-Gln. This is the combination yielded by human normal γ chains after the same treatment. Clearly it would be desirable to have an amino acid analysis for each spot: we intend to obtain larger amounts of material to make this possible.

A visual comparison of electrophoretograms derived from FcY-like protein and whole γ chains revealed that the relative intensities of staining of the three spots, all in fact approximately equal, were similar in each case; on the basis of 40% of the γ chain population bearing N-terminal PCA²⁴ approximately 8% of the FcY-like protein appears to bear it.

The above results demonstrate among the FcY-like protein a species which resembles γ CD protein by the three criteria which we set out. We shall call it partially deleted γ chain. Then the FcY-like protein has at least two com-

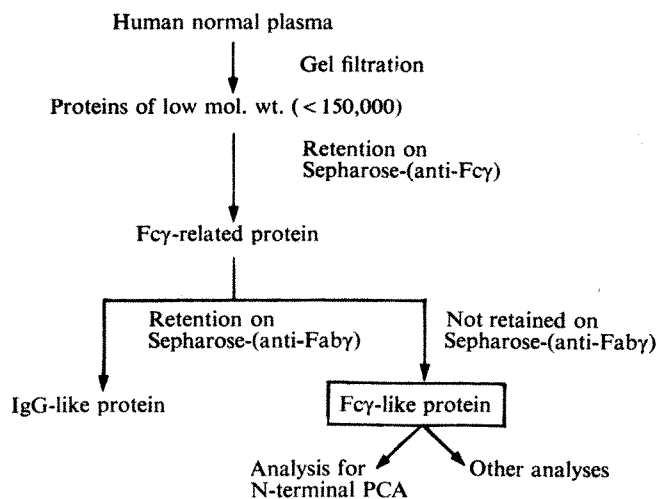


Fig. 2 Preparation and characterisation of FcY-like protein from human normal plasma. Pooled normal human plasma from a transfusion centre was defibrinated, and its proteins fractionated by gel filtration on Sephadex G-100 equilibrated with 0.1 M NaCl–0.02 M Tris-HCl (pH 8.0)–0.001 M Na₂EDTA–0.003 M NaN₃ (abbreviated below to Tris-NaCl). The 4S protein fraction, containing proteins of molecular weight less than 150,000, was passed through diethylaminoethyl cellulose to remove most of the plasma albumin and then concentrated by ultrafiltration. Further purification was by immunoadsorption. Immunosorbents with a Sepharose 4B matrix were prepared according to Cuatrecasas¹⁹, with the IgG fraction of the appropriate antiserum being coupled at pH 6.5. First, the proteins of low molecular weight were passed through blank (activated and deactivated) Sepharose 4B to remove any material adhering simply to the matrix. Next they were passed through Sepharose 4B-(rabbit anti-human FcY), binding all protein antigenically related to FcY. After washing the immunosorbent with buffer the FcY-related protein was eluted with 1 M NH₄OH, pH 11.7 (ref. 20). Some rabbit antibody leached out by this procedure was removed by passage at neutral pH through Sepharose 4B-(sheep anti-rabbit IgG).

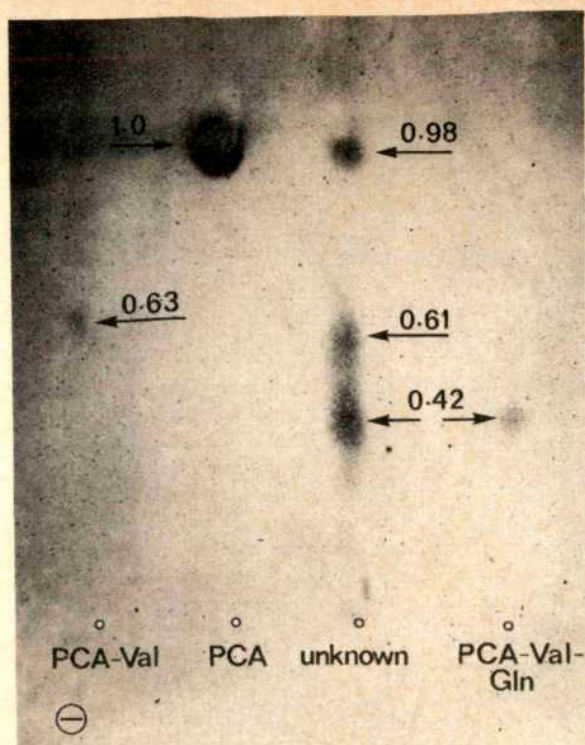


Fig. 3 Analysis by high-voltage thin-layer electrophoresis of material from the Pronase digest of Fc γ -like protein, not retained by cation-exchanger Dowex 50X2. Origins are indicated by small circles at the bottom of the photograph. The numbers are mobilities relative to that of the PCA standard. The three main spots given by the unknown sample have, within experimental error, mobilities equal to those of PCA, PCA-Val, and PCA-Val-Gln.

ponents: catabolically produced Fc γ ²⁶ and partially deleted γ chain. The proportion comprised by the latter, assuming that it resembles normal γ chains in having 40% of its molecules bearing N-terminal PCA²⁴, is very roughly 20%.

The following possible artefacts were considered and eliminated. First, that PCA originated from contaminating Faby-containing material. From model experiments we found that the maximum amount of Faby that could have escaped detection by the Ouchterlony technique would not have sufficed to give visible PCA spots on the electrophoretogram. Second, that PCA came from contaminating rabbit IgG. Again no significant contamination was picked up by Ouchterlony analysis, and in any case PCA-Val and PCA-Val-Gln would not be expected. Third, that PCA originated from cyclisation of N-terminal glutamine²⁵, *in vivo* or *in vitro*, in Fc which had arisen from catabolism of plasma IgG. No known IgG sequence²⁷ would also yield PCA-Val and PCA-Val-Gln. Authentic Fc γ put through our preparative and analytical procedure failed to yield any spots on the electrophoretogram. Conversely, significant underestimation of the PCA content due to opening of the ring²³ in the 1 M NH₄OH used for eluting from immunosorbents was eliminated by showing that incubation of γ chains in 1 M NH₄OH for up to 6 h at room temperature made no detectable difference to the yield of PCA.

At this stage we can make no reasonable estimate of the amount of partially deleted γ chain in normal plasma. We seem to have recovered about 2 mg from 12 l of plasma, but the preparative losses were enormous: probably >90%. It should be pointed out that the chance of one of our fifty apparently healthy donors having harboured unsuspected γ CD, with a known world total of only about thirty in 10 yr, is negligibly small.

The presence of normal protein analogous to γ CD proteins does not necessarily imply that each pathological

protein has a precise normal counterpart. For example it might merely reflect the occurrence of certain genetic accidents¹⁸ in normal as well as neoplastic lymphocytes: so that while DNA sequences encoded in pathological proteins should have precise counterparts, deletions need not. We do submit that deletions in γ CD proteins cannot now be attributed to some perturbation peculiar to the neoplastic process.

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Isolation of Fractions rich in Human Y Sperm

RESEARCH into the isolation of human X and Y sperm is now feasible because of the fluorochrome quinacrine that stains the Y chromosome^{1,2}. It is still impossible to identify the Y chromosome in sperm of other mammals, with the possible exception of gorilla sperm³, but when human sperm are stained with this fluorochrome and viewed under fluorescence microscopy, approximately half of them reveal a Y body. The Y body is the distal end of the long arm of the Y chromosome and shows up as a bright fluorescent dot⁴. The ability to identify the Y chromosome makes possible the collection of data on X and Y sperm^{5,6}.

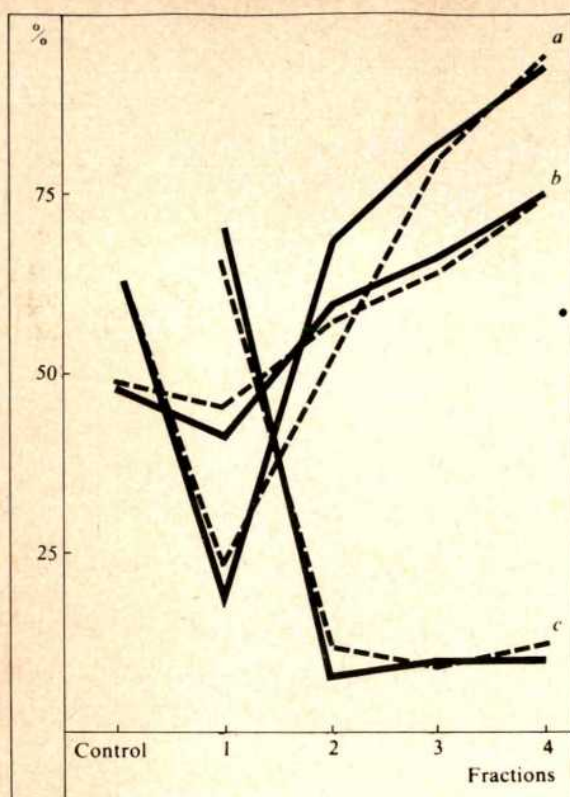


Fig. 1 —, Human sperm layered over a column of 6 and 15% BSA. Fraction 1 is the top sperm layer; fractions 2 and 3 are upper and lower halves of 6% BSA; fraction 4 is 15% BSA. Each line represents the mean of nine experiments with five different donors. (Two similar experiments where ovalbumin replaced BSA gave comparable results.) ---, Human sperm layered over a column of 10, 15 and 25% BSA. Fraction 1 is the top sperm layer; fraction 2 is 10% BSA; fraction 3 is 15% BSA; fraction 4 is 25% BSA. Each line represents the mean of thirteen experiments with five different donors. *a*, Motility; *b*, Y sperm; *c*, recovery.

Human sperm bearing a Y chromosome isolate from sperm bearing an X chromosome when layered over a medium consisting of bovine serum albumin (BSA) or ovalbumin. The basis for isolation is progressive sperm motility⁷, without which isolation of Y from X sperm does not occur. We can isolate repeatedly up to 85% Y sperm, of which 90 to 98% are progressively motile. Aside from considerations of fundamental biology, the isolation procedure is one that adapts to practical application.

The semen comes from seventeen paid volunteers born between 1935–56, some donating semen weekly for 21 months and others for a shorter period. The ejaculates are obtained through masturbation a few hours before use and fulfil the usual criteria for normalcy.

Semen, diluted 1:1 with Tyrode's solution, is centrifuged at room temperature for 15 min at 4,000 r.p.m. and the spermatozoa are then resuspended in Tyrode's at 100×10^6 ml⁻¹. Spermatozoa are checked for percentage motility and the degree of progressive motility⁸ at the start and again in each isolation fraction. Numbers of sperm are determined with a haemocytometer; total sperm recovered do not usually equal 100%, but the error factor is normally no greater than 15%.

The isolation procedure is a simple one in which an albumin in Tyrode's (crystalline BSA or a 25% concentrate in sterile Tyrode's (Sigma); crystalline ovalbumin (Miles-Seravac)) is placed in a glass column. Overlying the albumin is a standardised amount of sperm (50×10^6) in 0.5 ml of Tyrode's. The column is a Pasteur capillary pipette heat-sealed at the point of tapering. The basic one step experiment consists of 0.9 ml of a 3 to 25% concentration of

albumin, pH 7.4 to 7.6, overlaid with sperm. Spermatozoa in the top layer are pipetted off the underlying albumin medium (now also containing sperm) after 1 h. Spermatozoa from top and isolation fractions are then processed through the above-mentioned procedures. A second approach is to use two or three isolation steps, each one with higher concentrations of BSA. This process requires that spermatozoa swimming into the BSA medium be recovered by centrifugation and relayered again (same volume and number) over fresh medium with greater amounts of BSA. Replicate columns are used to increase workable sperm numbers for second and third step isolations. Again, 0.9 ml of albumin medium is used and each step of the experiment is stopped after 1 h; BSA concentrations normally are 6, 10 and 20%. The two or three step procedure is modified to a one step procedure by layering discontinuous gradients of albumin within the same column. A 15% albumin medium (0.4 ml) is overlaid with 0.8 ml 3 or 6% albumin. Spermatozoa in Tyrode's again make up the top layer. Another experiment is carried out by

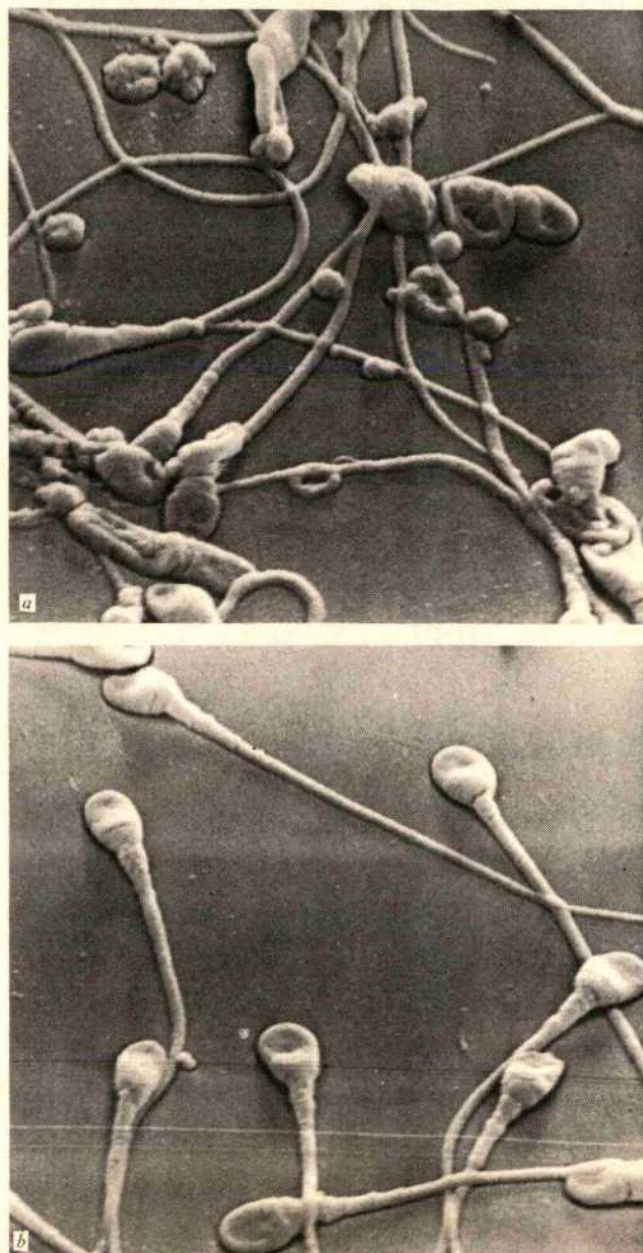


Fig. 2 Scanning electron photomicrographs of human sperm $\times 1,420$. *a*, Fraction 1 (see Fig. 1, solid line); *b*, fraction 4.

layering decreasing gradients of 25, 15 and 10% BSA over one another in 0.3 ml volumes. With multiple layers of albumin, the original sperm layer is still pipetted off after 1 h. The underlying gradients are, however, given additional isolation time of 30 min (two concentrations of albumin) or 60 min (lower two gradients of the three-tiered BSA concentrations). Routinely, spermatozoa in the various isolation fractions are washed 3 to 6 times in Tyrode's to prepare them for staining.

Sperm prepared for counts on Y bodies are air-dried on microscope slides and then stained with quinacrine dihydrochloride (Sigma); in most cases samples are fixed in methanol first. After many months of following literature procedures¹ we converted to the semiquantitative procedure used by Pearson (personal communication) where the stain is solubilised in methanol at approximately 0.5 to 1.0% concentration. Staining of sperm takes a varying number of minutes, depending largely on the fraction of origin. The slides are then put through two rinses of distilled water, fitted with a sealed cover slip and viewed under a fluorescence microscope. We use a Zeiss photomicroscope equipped with a high pressure mercury vapour lamp, BG 12 and BG 38 exciter filters and 440 and 470 nm barrier filters. Sperm are viewed under oil with a darkfield condenser at $\times 1,000$ magnification.

Table 1 Identifying Human Spermatozoa bearing the Y Chromosome

Total number of sperm counted	40,334
Total number of Y sperm counted	19,564
$\bar{X}$ % Y sperm	48.50
95% confidence limits *	48.26 to 49.31

* Calculated from counts made by one person (34,721 total; 16,939 Y sperm).

Control counts of Y sperm from 116 experiments are listed in Table 1. The arithmetic mean for Y sperm approaches the theoretical value and the 95% confidence limits fit well within values needed for reliable technique. Counts on Y sperm do not differ significantly ($P < 0.05$) within donors, between fourteen donors or according to the time of year. Inability to identify approximately half of the sperm as Y bearing or inability to obtain consistent results would call into question the accuracy of the experimental data. As our method for identifying Y sperm is indirect, this in itself increases the need for reliable control values. We routinely count 600 sperm both from the control and from each experimental fraction.

We are confronted with three explanations for the preponderance of 'Y bodies' in experimental fractions of the isolation column. The differences may be due to human bias, treatment artefact, or actual change in X and Y ratios. We believe we have satisfactory explanations to discredit

the first two possibilities, thereby supporting the third. Human bias (seeing Y bodies that in reality do not exist) can be discounted by always running a control sample, by having more than one person count each sample, and by coding the samples. The two counters (C. N. L. and R. J. E.) have, after considerable experience, compared counts on sixty-one different sperm samples and their results are statistically consistent², that is to say, neither counts more or less Y bodies. Treatment artefacts which might increase what appear to be Y bodies are more difficult to disprove. By exposing sperm to an isolation medium (BSA in Tyrode's solution) without attempting to isolate X and Y sperm, and by using non-motile or low motile sperm where isolation does not occur, we reaffirm our belief that BSA does not, in itself, cause sperm artefacts similar to Y bodies. However, final proof of an increase in frequency of Y sperm must await sexing of offspring conceived of spermatozoa exposed to the isolation process, whether this be in human or other species.

We started our research in X and Y isolation by layering spermatozoa over bentonite. Next we added BSA to the bentonite and eventually BSA without bentonite. We performed more than 110 BSA-only experiments and all succeeded in that progressively motile sperm, of which the majority are Y bearing, moved into the BSA medium. Our point is adequately made in Tables 2 and 3 and Fig. 1. Here we present the results of sixty-four experiments that typify the response of motile sperm to different concentrations of BSA and ovalbumin. We have focused our emphasis on increases of Y sperm in various fractions of albumins. A simultaneous increase in the percentage of motile sperm is also evident (Tables 2 and 3 and Fig. 1). In essence, the process successfully selects a population of spermatozoa that are predominantly Y bearing, almost entirely progressively motile and physically fit. Their homogeneous order results from the selection process where non-motile and many morphologically abnormal forms are excluded (Fig. 2). A logical clinical application of the 'cleaned up' sperm fraction would be in the artificial insemination of subfertile cases.

Sperm recovery (the number that enter albumin fractions) is dependent on progressive sperm motility and albumin concentration plus the added factor of time, which we have not yet adequately tested. The distance sperm must travel is also a factor, but, because the sperm are under gravity, non-motile sperm will with time move in the same direction. We therefore keep sperm recovery to around 25 to 35% by regulating sperm numbers, time and albumin concentration. Figure 1 is offered as evidence that the isolation process is consistent for values obtained, provided sperm have normal progressive and percentage motility. Replicate columns easily provide 10×10^6 to 50×10^6 highly active sperm thought capable of normal fertility. No evidence is available on human sperm fertility, but rabbit sperm subjected to similar isolation processes are fully fertile. In

Table 2 Isolation of Y Sperm with Different Concentrations of Albumin

Composition of isolation fraction	No. donors	No. experiments	% Y sperm*			% Sperm motility*			% Sperm recovery
			Washed sperm (control)	Top fraction	Isolation fraction	Washed sperm (control)	Top fraction	Isolation fraction	
3% BSA	3	7	50 $\pm$ 1	49 $\pm$ 1	57 $\pm$ 1	61 $\pm$ 3	27 $\pm$ 3	85 $\pm$ 2	40
5% BSA	3	8	49 $\pm$ 1	45 $\pm$ 3	64 $\pm$ 2	69 $\pm$ 2	26 $\pm$ 2	92 $\pm$ 1	27
6% BSA	3	6	49 $\pm$ 1	47 $\pm$ 2	63 $\pm$ 2	68 $\pm$ 3	19 $\pm$ 3	91 $\pm$ 2	29
7% BSA	2	2	50	—	64	63	38	83	34
10% BSA	2	2	48	45	61 $\dagger$	73	25	75	29
10% Ovalbumin	2	2	46	41	63	50	35	83	18
20% BSA	1	2	49	46	67	68	35	95	22
25% BSA (1-2 h)	4	7	48 $\pm$ 1	42 $\pm$ 2	65 $\pm$ 3 $\dagger$	66 $\pm$ 4	25 $\pm$ 5	90 $\pm$ 4	27

* Mean values $\pm$ s.e. $\dagger$ Lower half of isolation fraction

Table 3 Y Sperm Yield with a Two or Three Step Isolation Process*

Fractions	Two step isolation, two donors twice †			Three step isolation, one donor twice †		
	% Y sperm	% Sperm motility	% Sperm recovery	% Y sperm	% Sperm motility	% Sperm recovery
Washed sperm (control)	50	63		48	72	
Top fraction No. 1	45	20		46	12	
Isolation fraction No. 1 (6% BSA)	66	93	31	64	85	26
Top fraction No. 2	48	53		—	45	
Isolation fraction No. 2 (10% BSA)	76	98	44	68	95	52
Top fraction No. 3				—	86	
Isolation fraction No. 3 (20% BSA)		•		85	98	44

* % Y sperm in isolation fractions (Tables 2 and 3) are significantly greater ($P < 0.01$) than corresponding control values.

† Mean values.

this paper we stress the simplicity of this experimental procedure, repeatability of results and practicality of application to humans and perhaps other mammals.

Although we have discovered a practical way to isolate Y sperm, we have not achieved comparable results with X sperm at the same time, even though this finding seems biologically unlikely. The reason is that not all sperm participate in the isolation process and those that do so isolate in a manner that predisposes a like isolation of X sperm. Referring again to the work of Roberts⁷ the gravitational separation of motile human sperm is explained in mathematical models by the superior swimming ability of Y sperm as a function of time. As only 25 to 35% of the original spermatozoa enter the isolation medium and as the isolation process is a factor of time, distance and different viscosities of media, a comparable isolation of X sperm is impossible. Although the top sperm layer does contain an excess of X sperm (Fig. 1), it is only because more of the Y sperm swim out. The excess X sperm fraction is problematical in that it also contains most of the non-motile and abnormal sperm.

Our experimental results and empirical thought lead us to believe that by this process Y sperm isolation is dependent on overlaying of washed motile sperm in a vertical column, thus orientating a swimming movement downward; suspending sperm in a physiological vehicle of density lower than the isolation medium; making the difference in viscosity between sperm vehicle and isolation medium great enough to provide a formidable barrier at their interface; creating the interface such that it separates motile from non-motile sperm, morphologically normal from abnormal forms and starts the Y sperm isolation and extending the swimming distance and isolation time to a point where the now more prevalent Y sperm can continue to outdistance their remaining X sperm counterparts. Therefore, motile Y sperm can be said to have greater ability to penetrate an interface between fluids and between discontinuous gradients of an isolation medium. Y sperm must also swim faster than X sperm under the handicap of swimming in a fluid with, in relative terms, high density and high viscosity. Thus, we believe our concept in this paper breaks tradition with other experimental approaches to the separation of X and Y sperm¹⁰.

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Gastrin Activity in the Chicken Proventriculus

Reaumur and Spallanzani¹ used birds as experimental animals in the early days of digestive physiology; other workers on avian gastric digestion include Cheney², Friedman³ and Long⁴. The bird lacks the gastric antrum analogous to that in the mammalian species and there is a tubularly shaped glandular stomach called proventriculus which produces the gastric juice⁵⁻⁹. Unlike mammals, which have a separate HCl and pepsin-producing cells⁵, birds produce HCl and pepsin from the same gastric cells called oxynticopeptic cells⁵⁻⁹. These cells are arranged in tubular glands organised in lobules deep in the proventricular mucosa with central collecting cavities which open on the mucosal surface through ducts^{5,6}.

A comparison of the gastric secretion of the chicken to man, dog, rat and monkey revealed that the chicken secretes considerably more acid and pepsin in the basal state and following histamine (on a weight basis) than secreted by those mammals listed above⁴.

So far no reports of gastrin activity in the proventriculus nor attempts to extract this hormone from the specialised glandular stomach have been found in the literature. This work was done to detect and assess gastrin activity in extracts of the proventriculus and the duodenum.

Thirty-one healthy male white Leghorn chickens each weighing between 2 to 2.5 kg were used. Ten birds were killed at a time, and their proventriculi and duodenum (10 inch down the small intestine from the junction with the gizzard) were removed. The tubularly shaped proventriculi and the duodenal pieces were cut open and washed clean with water. Each proventriculus weighed between 3.5 to 4 g.

Ten proventriculi and ten duodenal pieces were separately weighed, cut into very small pieces, minced thoroughly and then subjected to the gastrin extraction procedure of Blair *et al.*¹⁰. Thus, there were three occasions when ten birds were killed; the remaining one bird was killed separately and the single duodenum was subjected to the gastrin extraction procedure.

The extracts were dried and their weights per g wet weight of the proventriculus and the duodenum were determined

and duodenal extracts. The resulting weights were used to calculate the mean weight of the extract per g wet weight of the proventriculus and duodenum.

Solutions of known concentrations of the powdered extracts were prepared using 0.9% NaCl solution as the solvent and the precipitates obtained after centrifuging for 10 min at 2,500 r.p.m. were discarded.

The saline solutions of the crude extracts were assayed for gastrin activity by using a modification of the continuous stomach perfusion technique described by Ghosh and Schild¹¹. Male Wistar strain rats weighing 180 to 210 g were used. The rats were anaesthetised with urethane (in 25% w/v solution given intraperitoneally at 0.6 ml per 100 g body weight).

The stomachs of the rats were perfused with saline (0.15 M) warmed to the rat's body temperature and the flow rate of the perfusate into the stomach was adjusted to give an effluent volume of 1 ± 0.1 ml min⁻¹. The effluent was collected at 10 min intervals and titrated to pH 8.8 with the Automatic Titrator (Radiometer, Copenhagen) using a centinormal sodium hydroxide as the base. This pH enabled the calculation of the total titratable acid in the collected effluent.

The following graded doses of the saline solutions of the proventricular and duodenal extracts, 250 µg, 500 µg, 1,000 µg and 2,000 µg, and of synthetic human gastrin I (SHGI), 15.75 ng, 31.5 ng, 63.0 ng and 126.0 ng, were injected intravenously through the femoral vein into the anaesthetised male rats. Injected doses of the saline solution of the proventricular extract and SHGI caused increased acid secretion whereas injected doses of solutions of the duodenal extracts produced no increase in acid secretion. The saline solution of the extract from the single duodenum was completely injected intravenously into the prepared rat at once and it produced no rise in acid secretion. The mean rates of acid secretion in µEq per 10 min to the injected doses of the stimulants were calculated according to the method of Lai¹². The log dose-response data showed parallel straight lines for the 500 µg and 1,000 µg of the saline solution of the proventricular extract and 31.5 ng and 63.0 ng of the SHGI. These doses were then used for the 2+2 (four dose) assay procedure.

The minimum dose of histamine which elicited acid secretory activity was determined on the anaesthetised rat preparation and was found to be 8 µg histamine dihydrochloride.

The crude extract from the proventriculus was 19.86 ± 2.38 mg per g wet weight of the proventriculus. When 500 µg and 1,000 µg of saline solution of the proventricular extract were injected intravenously, the mean rates of acid secretion were 2.52 ± 0.27 and 4.97 ± 0.46 µEq per 10 min (mean $\pm$ s.d. in six rats) respectively. The period of response to both the low and high doses of the SHGI and the saline solution of the proventricular extracts lasted between 30 to 40 min and the highest rate of secretion per 10 min was obtained during the second 10 min collection after the injection. The histamine content of the saline solution of the proventricular extract was 40.25 ± 2.5 ng per mg extract, using the isolated guinea pig terminal ileum¹³. The lowest dose of the saline solution which elicited acid secretory response was 62.5 µg. This dose contained about 2.5 ng histamine which was less than 1/300 of the minimum dose of histamine salt that produced acid secretory response on the rat preparation.

The gastrin activity detected in the proventricular extract was equivalent to 109.38 ± 2.5 ng SHGI per mg extract or 8.69 µg SHGI per proventriculus. The gastrin activities of the pyloric antral extracts of the following mammalian species expressed as SHGI equivalent were as follows: cattle, 55.03 ± 5.04 ng per mg crude extract; sheep, 57.1 ± 5.07 ng per mg crude extract; goat, 58.05 ± 4.55 ng per mg crude extract. The gastrin content of the chicken proventriculus per kg body weight expressed as SHGI equivalent was 3.475 µg whereas the cattle antral pyloric gastric content was 0.604 µg per kg body weight and the values for sheep and goat were 0.904 µg and 1.635 µg per kg body weight respectively. This work identifies the proventriculus as a source of gastrin in birds.

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Morphine-induced Suppression of Voluntary Alcohol Drinking in Rats

A DEBATE has arisen over whether there is a relationship between alcohol and morphine addictions. With the classical phenomena associated with addiction there is little or no evidence for a connection between the two drugs¹⁻⁴. The short-term effects are different, the withdrawal symptoms are different, morphine antagonists do not precipitate withdrawal in alcohol-dependent animals, and usually no cross-dependencies or cross-tolerances have been found, although there are reports of increased tolerance for morphine in mice that have been habituated to alcohol⁵ and in some human alcoholics⁶.

In contrast, there is evidence for a connection between the systems influencing the voluntary consumption of morphine and alcohol. In humans, it has been noted that many opiate addicts have had earlier problems with alcohol drinking, and often take large amounts of alcohol when narcotics are not available^{7,8}. In animals at least, the connection apparently has a genetic basis. A strain of rats specifically bred for high morphine consumption was found to drink more alcohol than a strain bred to ingest little morphine⁹. C57Bl mice are known to drink more alcohol than do CBA/Ca animals, and have been shown to drink more morphine solution also¹⁰. Thus animals, and perhaps humans, who are predisposed to consume higher amounts of one of the two drugs are often more likely to ingest large amounts of the other.

The present studies were designed to see if morphine itself would also affect the system regulating alcohol intake. We first tested whether a single morphine injection would influence concomitant alcohol drinking by rats that had had prolonged previous access to ethanol. Nine male Wistar-derived rats were individually housed in galvanised wire

mesh cages, under a 12 h light, 12 h dark schedule, with free access to a 10% (v/v) ethanol solution, tap water and the standard Alko food. After 141 d, five rats (mean weight=384 g) were injected intraperitoneally with 60 mg kg⁻¹ of morphine as the hydrochloride. During the 10 d prior to the morphine injection these rats drank a mean of 16.3 ml of alcohol solution per animal d⁻¹. On the first day after the injection, consumption dropped to 6.8 ml. Water drinking did not change significantly. The ratio of ethanol solution to total fluid intake, E/T, declined from 0.624 to 0.274 ($t=4.33$, 4 d.f., $P<0.02$). Alcohol drinking remained generally depressed for the first week after morphine administration. It was significantly ($P<0.02$) lower than the pre-injection level on the first, second, fifth, and seventh days after morphine was given, and only returned to the previous level 9 d afterwards. The four control rats, which were injected with a similar volume of saline, did not alter their alcohol intake.

Figure 1 shows the results of a replication of this experiment in which measurements were also taken of the daily food consumption. As previously, the alcohol intake was sharply suppressed and remained reduced for several days. In contrast, food consumption was not depressed as strongly and returned to normal more rapidly. Water drinking again was not suppressed at all.

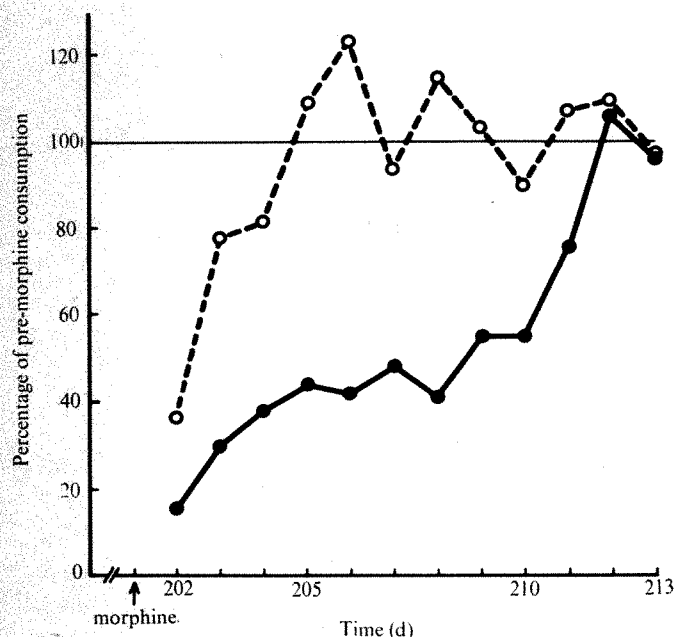


Fig. 1 Relative suppression of, ○, eating (g), ●, drinking of 10% alcohol solution (ml), after a 60 mg kg⁻¹ morphine injection. The data are from four male Wistar-derived rats, with a mean weight of 435 g at the time of the injection. They had previously had 201 d of free access to alcohol, plus food and water.

To test the specificity of the suppression to alcohol, five rats (mean weight=392 g), after 200 d of access to 10% alcohol solution and water, were given a third bottle containing a 0.013% (w/v) sodium saccharin solution for 10 d before a 60 mg kg⁻¹ morphine injection. Perhaps because of their prolonged previous experience with alcohol, the rats compensated for their saccharin consumption (11.6 ml per rat per d) primarily by decreasing their water intake from 17.7 to 5.9 ml per rat per d ($t=4.40$, 8 d.f., $P<0.005$), while alcohol intake remained nearly constant, going from 10.5 to 9.2 ml per rat per d ($t=0.67$). On the first day after the morphine injection, alcohol intake dropped to 1.4 ml per rat

($t=4.74$, 8 d.f., $P<0.005$), while water and saccharin drinking remained approximately the same as before the injection, at 6.6 ($t=0.27$) and 11.2 ($t=0.06$) ml per rat. Subsequently, alcohol consumption slowly returned to normal as in the previous experiments. The mean intakes of water and saccharin did not differ significantly from the levels observed before morphine administration. The morphine injection produced greater variability and instability in the consumption of water and saccharin. Only alcohol intake, however, was consistently suppressed.

We have also found that morphine given during a period when alcohol was withheld affects what has been called the 'alcohol-deprivation effect': if rats that have had prolonged access to alcohol are deprived of it for several days, they will temporarily drink much more alcohol than normal when access is first returned¹¹⁻¹⁶. Using conditions similar to those under which this effect has most often been observed^{12,13,16}, we administered morphine by different routes to three groups of male hooded Long-Evans rats during periods when they were without alcohol. One group (N=8, mean weight=465 g) with 81 d of access to 7% (v/v) alcohol solution was injected subcutaneously with 79.0 mg kg⁻¹ of morphine on the sixth day of an 8 d alcohol-deprivation period. The second group (N=7, mean weight=452 g) with 36 d of previous access was intubated with 10 ml kg⁻¹ body weight of 0.5 mg ml⁻¹ morphine solution on days 4, 5, 6, and 7 of an 8 d alcohol-deprivation period. The third group (N=8, mean weight=432 g) with 67 d of previous access was forced to drink a 0.5 mg ml⁻¹ morphine solution by making it the only fluid available on days 2, 3, 5, 6, 8, and 9 of a 10 d period without alcohol. When access to alcohol was returned, none of these groups showed a significant 'alcohol-deprivation effect'. In contrast, for each of these groups there was an appropriate control group, matched on previous treatment and pre-deprivation ethanol consumption level, which now showed a highly significant 'alcohol-deprivation effect'. For instance, after being forced to drink morphine during the alcohol-deprivation period, the rats' alcohol consumption changed from a mean pre-deprivation E/T of 0.524 to 0.483 ($t=0.38$). Alcohol consumption in the control group which was deprived of alcohol for the same duration, but was not given morphine, increased from E/T=0.521 to 0.852 ($t=4.77$, 7 d.f., $P<0.005$). Thus relative to the controls, the morphine groups showed a suppression of alcohol drinking. With the exception of the group intubated with morphine, to which a much smaller total dose of morphine was given, the relative suppression was of a magnitude and duration quite similar to that shown in the first three experiments in which alcohol was available when morphine was administered.

The groups receiving morphine all lost some weight as a result of the treatment. To test if this weight loss was responsible for the observed suppression of alcohol intake, three groups of male hooded Long-Evans rats were subjected to programmes of water or food restriction during alcohol-deprivation periods, such that the resulting weight losses covered the range previously shown by the groups given morphine. It was found that, unlike the morphine groups, each of these groups showed significant 'alcohol-deprivation effects', despite their weight losses.

Together these studies show that morphine, given by any of several routes, strongly suppresses alcohol consumption for over a week after its administration in at least two strains of rats, under a variety of experimental conditions. The suppression does not appear to be caused directly by the short-term effects of morphine intoxication, such as the reduction in motor activity and the inhibition of reflexes, which may interfere with drinking in the first few hours: the suppression lasts much longer than these effects, and other consummatory acts such as drinking water and saccharin solution are not suppressed. Nor is it an aversion to alcohol learned through its association with these short-term effects: the relative amount of suppression is the same when alcohol

is not present for association immediately after morphine administration. Similarly, it does not appear to be the result of alcohol being associated with morphine withdrawal sickness, in spite of a recent finding that during morphine withdrawal rats decrease their consumption of a novel saccharin solution supposedly because of such associations¹⁷. These associations tend to be formed with the most novel substance present¹⁸. In our experiment in which the rats had a choice between alcohol, saccharin and water, the alcohol was not as novel as the saccharin (210 d as against 10 d of previous access), and, therefore, if a learned aversion were the important influence, saccharin rather than alcohol consumption should have been suppressed. The weight losses following morphine administration do not seem to be responsible themselves for the suppression since similar weight losses induced by fluid or food restriction do not produce similar results. Finally, it does not appear to be caused by a loss of appetite for calories, since food consumption is not suppressed as severely or for as long as the alcohol drinking.

In summary, it appears that in spite of the difference between morphine and alcohol in terms of intoxication, tolerance and dependence, there are connections involved in the consumption of the two drugs: first, an apparent genetic correlation between predispositions to ingest them, and now a suppressive action of morphine on the drinking of alcohol. The mechanisms producing these interactions are still debatable, but the connections do exist.

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A Jumping Millipede

Most zoologists would consider a jumping Diplopod to be a highly unlikely animal. Whilst one of us (J. G. B.) was in Sierra Leone recently, however, he collected some millipedes which can perform a succession of four or five short hops. The millipedes belong to the sub-order Stemmiuloidea. The genus represented in Sierra Leone is *Diopsiulus* Silvestri, of which there are several species, all superficially similar, which all have this characteristic jumping behaviour. Cook¹, writing on neotropical species belonging to the sub-order, reported that the animals "frequently throw themselves several inches when disturbed", and wrote that the collector of a species in Ceylon (*D. ceylonicus*) reported to Pocock that the animals were saltatory. Cook wrote that the "apparent jumping motion is caused by vigorous wriggling of the body".

The jump is an escape reaction which can be provoked by touching a millipede. The unusual feature of this behaviour is that the animal usually jumps in the same direction as it runs. It jumps 2–3 cm, lands, slides, runs forward, jumps again, lands, slides, and so on. We filmed a series of such jumps performed by *D. regressus* Silvestri at 64 and 2,000 frames s⁻¹. The sudden body movement was shown to be a rapid humping of the body about one quarter of a body length behind the head. This hump becomes a loop which is then thrown upwards and forwards, dragging the posterior half of the animal after it (Fig. 1). The head and anterior leg segments remain stationary upon the ground until they are overtaken by the rapidly moving body loop, when they are also pulled forwards and upwards.

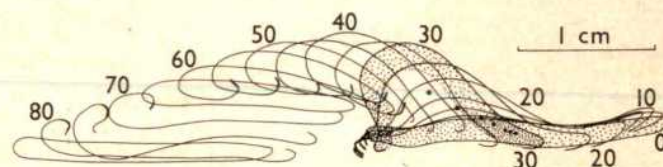


Fig. 1 Side view of a jump, from right to left, of the millipede *Diopsiulus regressus*. It is a composite based upon successive frames of a ciné film taken at 2,000 frames s⁻¹. Every tenth frame is shown, and the figures are in ms after the start of the jump. For most frames only the dorsal edge of the profile and the head and tail are shown (the head is indicated by a thickened line). The initial position (at 0 ms) and the position at take-off (30 ms) are shaded. The successive positions of the centres of gravity of each profile shown between the 0 and 30 ms positions are indicated by large black dots. They cover the acceleration distance. In this particular jump, the millipede rotates 180° about its longitudinal axis between take-off (at 30 ms) and landing (at 75 ms).

How is this jumping action produced? The stemmiuloids belong to the order Nematophora which includes the fastest running millipedes^{2,3}. A 2.3 cm long specimen of *D. regressus* can run at 5.6 cm s⁻¹, which is rapid for a millipede, a class which has specialised in slow, powerful pushing movements. When a nematophoran is running rapidly, a slight dorsal hump is seen over those legs which are moving forwards in the recovery phase⁴. This is due to the approximation of the sliding sternites by the action of powerful ventral muscles. This latter process may initiate a jump, although since the millipede halts momentarily before jumping, it must occur in a stationary animal. After the initial humping, the rapid production of a large loop is probably due to the contraction of the muscles that normally cause spiralling. The head and a few anterior leg segments remain turned forwards to maintain a grip upon the ground. (A millipede will not jump on a very smooth surface, apparently because it cannot maintain its grip.) The anterior limb of the loop is swung forwards about this fixed anterior point, and the posterior part of the body is dragged after it.

This jumping action moves the centre of gravity of the millipede rapidly forwards and upwards at an angle of about 27° (Fig. 1). In a typical jump, a 2–3 cm millipede was accelerated to a take-off speed of 48 cm s^{-1} over a distance of 0.72 cm in 0.03 s. This gave a ground level to ground level movement of the centre of gravity of about 2.5 cm (including horizontal movement during acceleration and horizontal movement during the return to ground level). The average acceleration during the jumping action was equivalent to 1.6g. Successive positions of the centre of gravity were estimated by cutting cardboard profiles of the millipede's positions at 0.005 s intervals during the jumping action. This rather crude analysis showed that accelerations fluctuated between 0 and 4g. When a smoothed distance-time curve was used as a basis for estimation, the accelerations determined were nearer the estimated 1.6g average. The maximum acceleration reached is probably not greater than about 2–3g. Since the acceleration used is relatively small for such a small animal, and the period of time available for the contraction of the muscles causing jumping is relatively large, a special catapult mechanism may not be necessary for the jump. There is a pause of only 0.03 s to 0.04 s between stimulation and jumping (that is, to frame 0 in Fig. 1). Whilst this is obviously sufficient time for the jumping reflex to take place, it is probably insufficient for much tension to be built up in the muscles antagonising the spiralling muscles (this being necessary for a catapult to operate). The millipede lands in a U-shaped position and normally falls onto its side. It usually swings the head forwards in about 0.05 s after coming to rest and then runs forward a short distance before the next jump.

The usual defensive movement shown by *Nematophora* (and, indeed, most millipedes) is a rapid spiralling of the body to enclose the head and legs. If this movement were restricted to the anterior half of the millipede, but the head and a few anterior segments remained turned forwards to maintain a grip on the substrate so that a loop formed in the vertical plane, it would produce a jump. Thus the unusual escape reaction of jumping seems to be closely related to the normal defensive reaction of spiralling.

We thank Charles Lowe of the Manchester University Engineering Photography Studio for undertaking the high speed ciné photography.

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Similarity of Bones and Antlers gnawed by Deer to Human Artefacts

THE anthropologist, when studying excavated bone remains, often finds it difficult to distinguish specimens worked by hominids from those damaged by other processes. Although damage by carnivores and rodents is widely recognised as a potential source of confusion¹, the role of herbivores (though well known to cattle and deer herders) is less well documented. In this communication, which originates from a visit to the Hardangervidda Mountains, Norway, in 1971, I describe some bones and antlers gnawed by Norwegian reindeer and Scottish red deer. It is clear that bones and antlers so gnawed can resemble human artefacts and have sometimes been mistaken for them.

In veterinary circles the ingestion of materials other than normal food is known as pica, the abnormal chewing of bones being osteophagia. Osteophagia has been discussed by many writers, for example Blood and Henderson², who point out that in herbivores it is often a symptom of phosphorus deficiency. This habit is widespread in natural conditions and has a distinct geographical distribution which depends principally on the phosphorus content of the parent rock on which food plants are growing, but also on other factors such as excessive calcium, aluminium or iron, which can reduce the availability of phosphorus to plants. Large areas of land in many countries are, in consequence, of little value for livestock without phosphorus supplementation. This can be achieved either by dressing pasture or by supplementary feeding of bone-meal and other forms of phosphate^{3,4}, or even by the crude provision of bones for chewing. Hagerty⁵ recorded a Scottish gamekeeper leaving the legs of a red deer, which he had shot, on a hillside for other deer to chew. Fraser Darling^{6,7} has described how, even before modern advances in the understanding of animal nutrition, the inhabitants of Atlantic townships of the Hebrides ground the backbones of fish (which accumulated as a byproduct of the fishing industry) to make a meal consisting largely of calcium phosphate, which was fed to the cows during the winter. In this way the lime-rich and phosphate-poor soils of the machair were able to support cattle. This industry has now disappeared and in the 1940s cattle were often seen beachcombing for bones along the shore.



Fig. 1 Captive muntjac deer, belonging to Dr O. Dansie of Welwyn, chewing a bone which is grasped by the left cheek-teeth in a "cigar-like" manner (photo by courtesy of O. Dansie).

The chewing of bones by artiodactyls is widespread. In addition to cattle it has also been observed, for example, among red deer, reindeer, muntjac deer, camels, giraffes, wildebeest, kudu, gemsbok and sable antelopes. Rolfe (personal communication) has described a cow eating a sheep skull on the Island of Skye in 1972; MacNally⁸ has recorded cross-bred highland cattle chewing bones, and figured antlers chewed by Scottish red deer, some almost down to the basal coronet; Lindgren and Utsi (personal communication) have mentioned similar chewing by red deer in the Glenmore area so that at the end of the winter antlers have completely disappeared; Teagle⁹ has described seeing a red deer chewing a rabbit carcass in Richmond Park; and Lord Cranbrook (personal communication) observed a red deer chewing its neighbour's antlers in County Donegal in 1927.

The chewing of antlers by reindeer (and the conspecific caribou of North America) has been recorded by various

writers including Millais¹⁰, Banfield¹¹ and Kelsall^{12,13} in Canada. Mitchell (personal communication) has observed reindeer chewing shed antlers near Abismo, Sweden; and Gaare (personal communication) records that southern Norwegian reindeer not only commonly chew shed antlers but sometimes also those on other reindeer. The most detailed description of gnawing by caribou is that of Kelsall who observed that in the Bathurst Inlet area of Canada it was unusual to find any antler, even large ones, which had not been chewed. Frequently antlers were reduced to stubby butts and those frozen into snow or ice were chewed down as far as possible. He also found evidence of reindeer chewing the bleached skulls, leg bones and vertebrae of reindeer and the long bones of other mammals including wolves and long-dead Eskimos. The area of study (personal communication) is calcium rich.

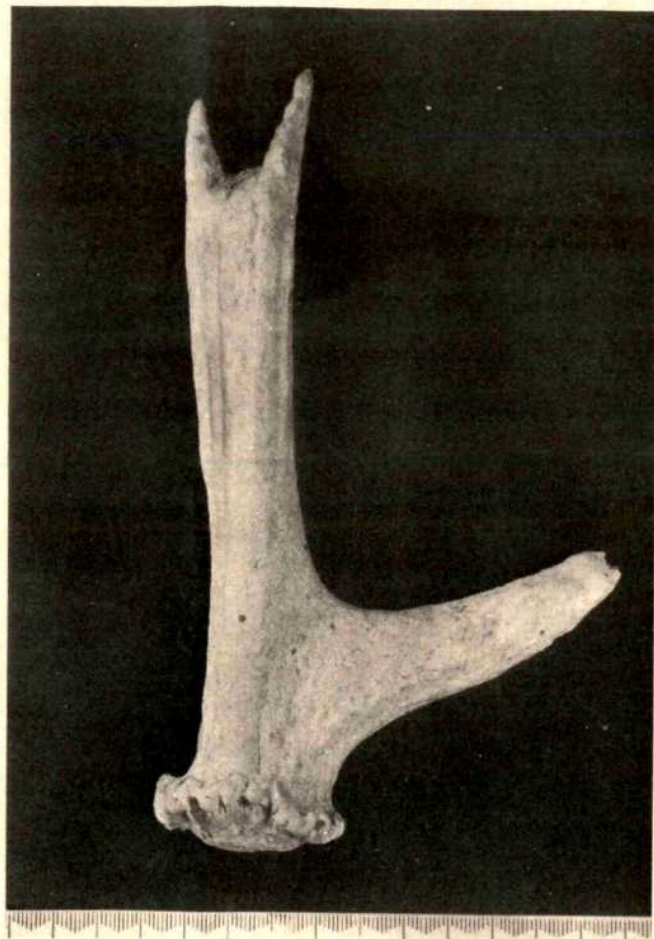


Fig. 2 Red deer antler chewed by wild Scottish red deer to create a "fork". Collected by L. MacNally (photo by courtesy of British Museum (Natural History)).

Dansie (personal communication, Fig. 1) described a captive doe muntjac deer picking up a bone in its mouth, though this was soon discarded unmarked. Cowles (personal communication) described two camels squabbling over a skeleton of a goat, already clear of flesh and skin, in the Jebel Faiyah Mountains of Oman (an area of barren rocky desert) in 1970. One camel was standing with its head in an upright position with the bones hanging out of its mouth. It was crunching the bones and swallowing the fragments. For a time both camels were grasping the remains. Evans¹⁴, Western¹⁵ and Wyatt¹⁶ have described the chewing of bones by giraffes at three localities in Kenya. The chewing of bones by wildebeest, kudu and gemsbok is known in the



Fig. 3 Reindeer metatarsal chewed by wild Norwegian reindeer to create "fork" with zigzag margins at its proximal end. Collected by the writer near Sandhaug, Hardangervidda Mountains, Norway, 1971 (photo by courtesy of British Museum (Natural History)).

Kalahari Desert (personal communication from Yellen) and by sable antelopes in the Simba Hills, Kenya (personal communication from Leakey).

The chewing of bones by artiodactyls can lead to injury or even death. Kelsall¹² has observed in Canada that caribou may continue to chew antlers until after this has caused bleeding about the mouth. MacNally⁸ records instances of a red deer with a sheep skull and another with a pelvic bone, which they had attempted to eat, wedged around their lower jaws. In some areas of Africa, where shortage of phosphorus in plants coincides with occurrence of the anaerobic bacterium *Clostridium botulinum* type D, cattle which chew the bones of animals dead on the range may die from botulism caused by poisoning by toxins present in associated decaying musculature (Riemann¹⁷; Smith and Jones¹⁸).

Since deer, like cattle and antelopes, have no upper incisors, they are dependent on their cheek teeth for any chewing which necessitates the use of opposing teeth. The chewing of bones by red deer and reindeer has been witnessed by various observers. MacNally (personal communication) has described seeing a Scottish red deer hind chewing a bone. This was held aslant in its jaws, not crossways, with about four inches protruding at an angle behind the incisors, while it chewed on the end with its cheek teeth. After a short time the bone was transferred to the other side of the mouth and chewing was continued on the cheek teeth of that side. Wheeler (personal communication) has given a similar account of a red deer hind chewing a bone (apparently a metapodial of a sheep or deer) near Cape Wrath, Sutherland, in 1966. The bone was held lengthwise in its mouth with more than half projecting forwards and a little to one side, "like a cigar". The bone was continually shifted from side to side. Dansie's photograph of the muntjac deer (Fig. 1) shows this animal holding a bone in a like manner. Kelsall¹² has described a

similar procedure by Canadian caribou, chewing being with a sideways movement of the jaws.

Most bones and antlers are oval and not exactly circular in cross-section. In consequence, when a deer holds one with its longest dimension pointing forwards and applies a sideways chewing movement, the object becomes oriented with its widest diameter across the width of the mouth. Continued chewing will plane off the top and bottom until the marrow cavity or antler core is reached, leaving only the sides intact. The fork-like remnants which result are a characteristic product of chewing by deer. Four series of examples will be described here. (1) Deer metapodial chewed by a red deer: well developed "fork" on both ends. Since this bone is dorso-ventrally flattened at its distal end, laterally at its proximal end, the "prongs" of the two forks are not in the same plane but are set as if rotated 90°. (2) Red deer antlers chewed by red deer. Less well developed "forks", the "prongs" being at the sides of the widest diameter (see Fig. 2). (3) Reindeer metatarsal chewed by a reindeer (see Fig. 3): the "prongs" of the "fork" are at the sides of the shaft. The remarkable zigzag (a feature first described in 1957 by Kelsall) matches the alternating upper and lower cheek teeth of the chewer (see Fig. 4). The perfection of this specimen is unusual. (4) Reindeer antler tines chewed by reindeer, showing a less well developed zigzag than (3) and some shredding. Kelsall (personal communication) has described finding many hundreds of bones and antlers similarly chewed by Canadian caribou. A description by Gordon of gnawing of antlers by Canadian caribou is in preparation.

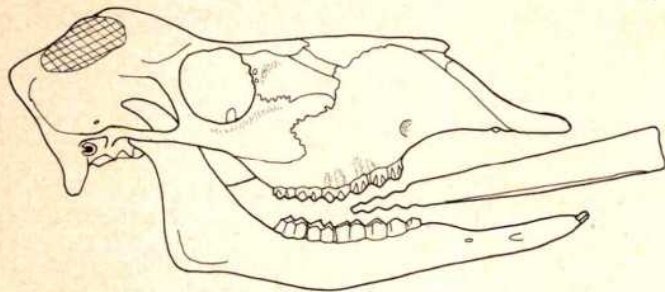


Fig. 4 Sketch showing relationship between the specimen shown in Fig. 4 and the cheek-teeth biting surfaces of a reindeer.

Since phosphorus deficiency in herbivores is unlikely to be a new phenomenon, evidence for it is to be expected in the palaeontological record. Antlers and bone remains of the pigmy deer, *Cervus cretensis*, of Pleistocene age, showing apparent deer chewing, have been collected by Sondaar from a cave west of Rethymnon, Crete (see Fig. 5). The occurrence of this phenomenon in a limestone area is in accordance with the known frequency of bone chewing by deer in calcium-rich areas today, as outlined earlier. Similar Pleistocene remains have been described from other Cretan localities by Kuss¹⁹, who attributed damaged antlers and bones of the same species of deer to an "osteokeratic culture" of Palaeolithic man. He figured fragments of antler, radius, ulna, metatarsal and mandibular ramus, all showing "forks" with "prongs" at the sides of their planes of flattening. There is some evidence of a zigzag pattern similar to that of the reindeer-gnawed specimens described earlier. The alternative interpretation, that these Cretan remains have, in fact, been chewed by deer, needs to be given consideration.

I thank L. MacNally and G. Kinns who provided antlers chewed by red deer and information; P. Sondaar who drew my attention to the Cretan problem and provided specimens; and A. W. F. Banfield, G. S. Cowles, Lord Cranbrook, O. Dansie, E. Gaare, B. C. Gordon, J. P. Kelsall,

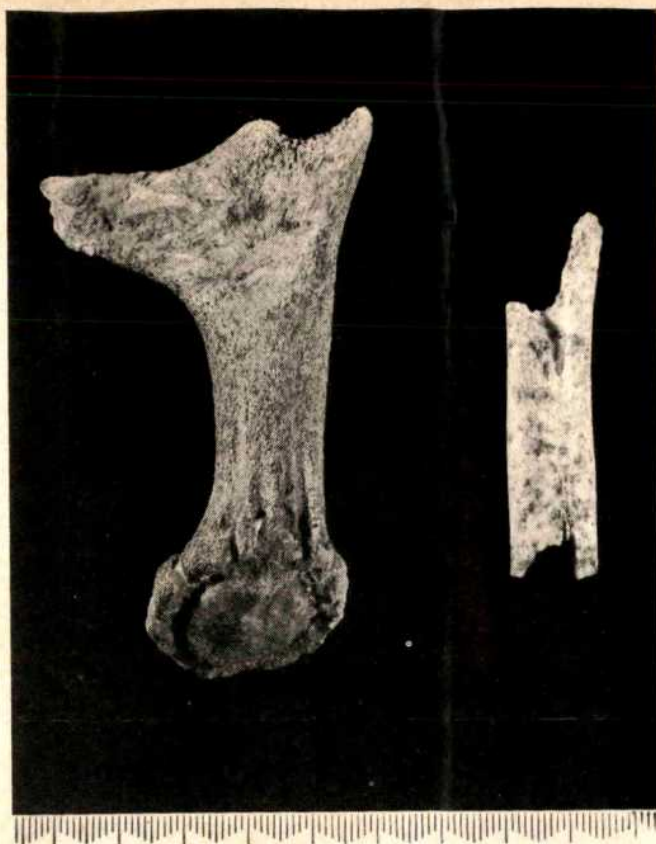


Fig. 5 Antler base and radius of the Cretan pigmy deer, *Cervus cretensis* (Pleistocene age) chewed by deer. Collected by P. Sondaar near Rethymnon, Crete (photo by courtesy of the British Museum (Natural History)).

Mrs L. S. B. Leakey, G. F. Mitchell, W. D. I. Rolfe, W. G. Teagle, E. J. Lindgren, M. N. P. Utsi, Miss E. C. Wheeler and J. Yellen who generously shared their own observations or provided information.

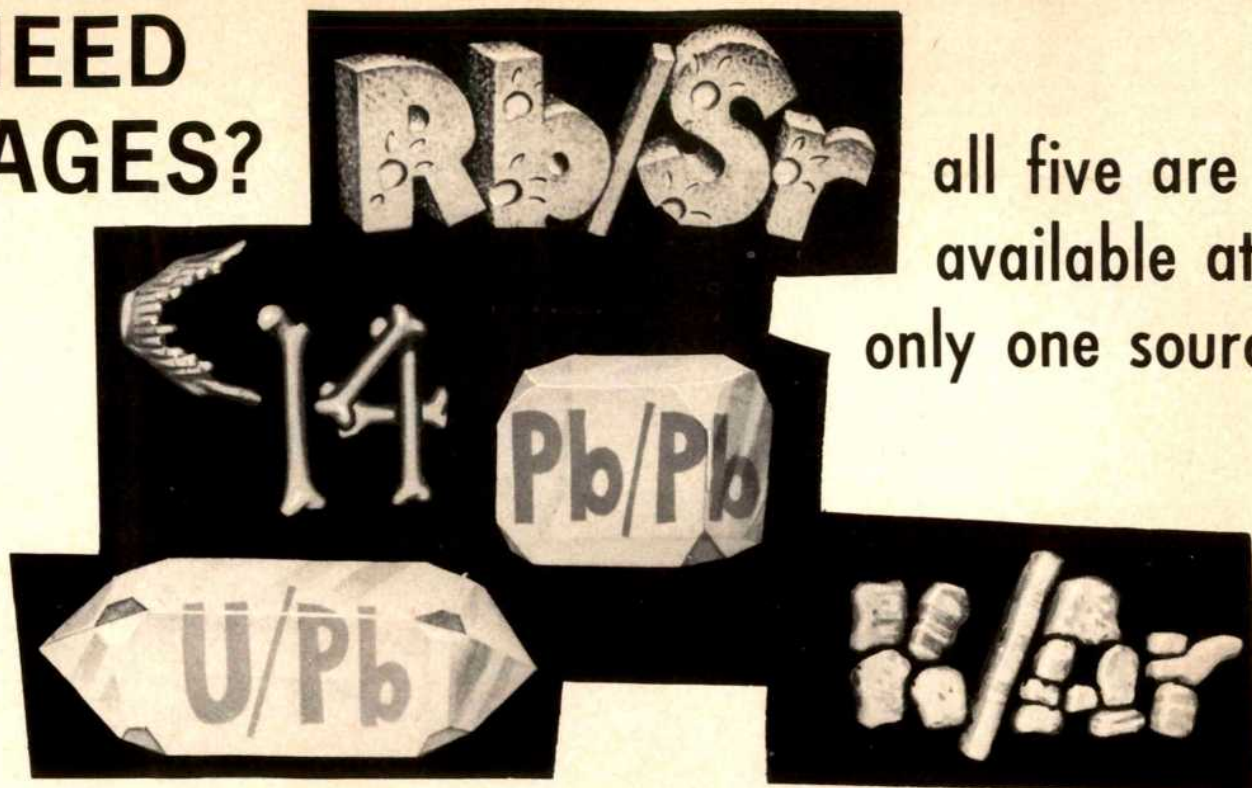
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BOOK REVIEWS

Einstein

Einstein: The Life and Times. By Ronald W. Clark. Pp. 670 (28 plates). (Hodder and Stoughton: London, September 1973.) £5.50.

If people who are not scientists are asked to describe their image of a scientific genius, the picture they paint seems more often than not to be based on a distorted memory of Einstein. The shaggy hair, the neglected appearance, the absentmindedness (presumably all induced by a complete devotion to scientific research) together with a general air of benevolence—this is what a real scientist should be like.

The first thing that R. W. Clark's new biography of Einstein does is to confirm that this popular representation fits the man quite well. Einstein truly paid little attention to his own appearance. His friend, Infeld, noted that Einstein always tried to minimise external distractions. "Long hair minimises the need for the barber. Socks can be done without. One leather jacket solves the coat problem for many years. Suspenders are superfluous, as are night shirts and pyjamas." Again Einstein was often absentminded: he was constantly mislaying his keys, even when taking his wife home after their wedding ceremony. Moreover, these characteristics did result from his devotion to science. The Universe came first, and everything else, including his own wife, came second. This latter circumstance was observed with some disapproval when he moved to the United States. "Your wife seems to do everything for you", observed one Princeton wife to Einstein. "Just exactly what do you do for her?" Yet the air of benevolence was also real enough. Even if the innumerable stories of helping children with their mathematics homework are apocryphal, they genuinely reflect something of the man.

This correspondence between the myth and the reality is typical of Einstein. When we move from the level of the popular image to consider Einstein as a major figure in the history of science, we find that at this level, too, he seems to provide a paradigmatic instance of the leader of a scientific revolution. If, for example, we look at the life of that other scientific genius, Newton, we can note the following points. Many of Newton's major concepts were worked out over a short period of time, while he was still a young man. In the latter part of his life, he produced no work of the same signifi-

cance. Finally, although he inaugurated a revolutionary change in science, his mode of thinking also showed a clearly conservative trend. (This was referred to by Keynes in his description of Newton as "the last of the magicians".)

If we now compare Einstein's development, we find that his major work was also concentrated into a short period of time when he was a young man. In 1905 he published papers on Brownian motion, the photoelectric effect and special relativity. All three were of fundamental significance for the evolution of physics. Einstein's name has become so inseparably linked with relativity that it is salutary to remember he was awarded the Nobel prize for his work on the photoelectric effect. Moreover, his work on Brownian motion effectively concluded a centuries-old debate on the nature of matter. At least one outstanding scientist—Wilhelm Ostwald—accepted it as the final, conclusive proof of the atomic theory.

It was, however, on relativity that Einstein subsequently concentrated, leading on to the publication of the General Theory during the First World War. Yet, again like Newton, his later life produced nothing of major scientific importance. During this latter period his own particular streak of conservatism also came to the surface. His virtually single-handed fight against indeterminacy—excellently described in this book—left him isolated in the world of physics. In 1935 he told an old friend: "In Princeton they regard me as an old fool".

Even in the interplay between science and the world of politics, Einstein seems a typical twentieth-century figure. He is the persecuted Jewish intellectual fleeing from Nazi oppression. He is the well meaning scientist drawn into the problems of war (and, according to Clark, rather more knowledgeable about the atomic bomb project than has generally been supposed). Finally, he is the scientist who, after the explosion of the first atomic bombs, recoils from what has been done, and works and speaks for methods of control.

This archetypal quality of Einstein's life reflects two things: first, the essential qualities required of a genius, but, second, the way he became—in Clark's words—"the conscience of the (scientific) world". It is with these aspects of Einstein that Clark's biography is concerned, rather than with a detailed critique of Einstein's scientific ideas (though he examines the general nature of these ideas and their recent history

with distinct skill). He has provided us with a massive and fully documented account which, in its main outlines, must surely be regarded as definitive.

This does not, of course, mean that the text cannot be faulted. In terms of sources, for example, although Wertheimer is mentioned in passing, his published account of conversations with Einstein in the period leading up to the General Theory is not included in the bibliography. Again, Clark is not always accurate in his background details. Thus he implies (page 224) that a Joint Permanent Eclipse Committee was specially set up in England for the solar eclipse of 1919. In fact, as the name of the committee implies, it had been established on a continuing basis long before.



[Ronan Picture Library]

Such omissions or ambiguities are rare; nor is there a large number of misprints. The most irritating aspect of the book is the complete lack of correlation between the text and the references. The latter, which are extensive, are collected together at the end of the book, but contain no indication of the page to which they refer. The text, on the other hand, provides no mention of the references at all.

It would be wrong, however, to end a review of this excellent biography on a note of criticism. Rather I should say that Clark puts forward certain general hypotheses concerning Einstein that would repay further examination. One concerns the reason for Einstein's displacement from the mainstream of physics: according to Clark, this derived in particular from a concentration on mathematics at the expense of physical reasoning. But the most important of these themes is declared in the foreword—that Einstein was "one of the great

tragic figures of our time". (This is one of the points where the analogy between Newton and Einstein breaks down: Newton could hardly be considered in any sense as a tragic figure.) Clark develops this statement throughout the biography. If it remains not entirely convincing at the end, this does not derive from poor exposition by the author. The difficulty stems more, perhaps, from Einstein's own single-mindedness. It is hard to discern the century's great tragic hero in someone who saw the Universe as so much more important than human activities.

A. J. MEADOWS

Aspects of the Earth

Topics in Geophysics. By P. J. Smith. Pp. x+460. (Open University: Bletchley, May 1973.) £2.50.

THIS is a textbook for a short course in geophysics given by the Open University. The book does not attempt to cover the whole subject but chooses three topics as representative of different aspects.

The first is the structure and physical properties of the Earth's crust and upper mantle as determined from seismology and gravity; this represents a largely factual account about whose conclusions there is little doubt. The next topic is the heat flow from the Earth and its thermal properties. This is a subject in which a considerable range of views is possible owing to the inaccessibility of the deep interior of the Earth to temperature measurement. The third topic is earthquakes with special reference to prediction and prevention; this is a subject with engineering and social implications.

In the context of the Open University the plan of the book seems very suitable. Their short course could not cover the whole subject, except in a very superficial way, and the presentation of three contrasting topics in some detail seems a good way of providing something with a real intellectual content to students who do not intend to become professional Earth scientists. Within the three topics the author has a severe problem of choosing what to put in and what to leave out, and agreement is not to be expected. To me it seemed that in discussing the Earth's crust there was too much emphasis on gravity and too little on the mechanisms of earthquakes, the study of which has so strikingly contributed to the understanding of plate tectonics.

The figures are nearly all reproduced from papers; many of them could have been greatly improved by redrawing and some are hardly intelligible (for example, the map showing Pacific guyots and that of Japanese earthquakes).

How far the book will find an audi-

ence outside the Open University it is difficult to say. It is interesting and worth reading for a schoolboy or an undergraduate with an interest in the Earth, but have they the time to read a book that confines itself to three selected topics? I hope they have.

E. C. BULLARD

Jodrell Bank

Out of the Zenith: Jodrell Bank, 1957-1970. By Bernard Lovell. Pp. 255 (8 plates). (Oxford University: London, Melbourne and Toronto, November 1973.) £5.50.

SIR BERNARD has made the hiatus caused by conversion work on the Jodrell Bank 250-foot Mark 1 radio telescope the opportunity for an account of what he likes to call his "stewardship of that unique instrument". Since he describes not only the scientific work but also the diplomatic and managerial activities that went on behind the scenes to keep the show on the road, many interesting issues arise that can only be touched upon in a brief review.

Although for most of 1957-70 the Mark 1 was the largest fully steerable telescope in the world, it was involved directly in few of the most spectacular radio astronomical discoveries of the period—quasars, the radio source counts, pulsars. The initiative in the study of discrete sources has remained firmly with the interferometers developed in the early fifties. This is mainly because, to achieve a resolution or positional accuracy comparable with optical telescopes, radio telescopes with overall dimensions of the order of miles, rather than hundreds of feet, are needed. Indeed in one of the most successful programmes pursued at Jodrell Bank, the study of the structure of extragalactic sources, the Mark 1 dish was itself used as one arm of an interferometer, the other being a variety of much smaller aerials at ever increasing distances. By 1962, using a baseline from Jodrell Bank to Lincolnshire, Henry Palmer and his group had surpassed the best resolution obtainable with optical telescopes (1" of arc), and by 1966 they had shown that a number of quasars have sizes smaller than a few per cent of this.

Had these studies continued throughout the sixties there could now be some structure information down to 1" or better for all the brighter sources, a task now being undertaken by the new Cambridge 5 km interferometer (which will provide complete maps of the sources). Instead, Sir Bernard describes how he diverted Palmer and his group to what proved to be the chimaera of intercontinental baselines with the Russians as the other end of the interferometer arm. An intercontinental link was eventually achieved in 1969 with the huge Arecibo telescope

in Puerto Rico, but some two years after the Canadians and Americans had been on the air.

The programmes to which a telescope like the Mark 1 is ideally suited are those pursued by the groups under R. D. Davies on the 21 cm hydrogen line (primarily the structure of our own Galaxy), under R. G. Conway on the accurate fluxes, spectra and polarisation of radio sources, and under Graham Smith on the pulsars. Curiously, Sir Bernard finds space to describe only the last of these three programmes, bowing no doubt to popular interest. Instead there is an account of what might be called 'radar games' in which the United States and the Soviet Union bounce messages of dubious goodwill to each other off the Moon, balloons and what have you, using Jodrell Bank as a sort of telephone exchange. Like the manned space programme, this was no doubt entertaining for the general public, at least on the first occasion.

Jodrell Bank has been *par excellence* a pulsar observatory and has discovered more than half the northern hemisphere pulsars known. The pulsars therefore deserve their three chapters in the book, although I frankly think that Graham Smith might profitably have been asked to contribute these chapters. Indeed, a more balanced and penetrating account of Jodrell Bank's scientific work might have been arrived at by asking Palmer, Davies, Conway and Smith each to contribute sections on their own programmes, with Sir Bernard providing those interesting glimpses of the committee men in action. That, of course, would not be Sir Bernard's style, and instead we get an account of pulsars which might have been satisfactory in 1969, but seems a bit thin on the observational side for 1973. And the only theoretical work described is Gold's now superseded 1968 model. No mention at all of Pacini's 'oblique rotator', now all the rage.

There is a chapter on Sir Bernard's own observational work on red dwarf flare stars, a topic which I found interesting and not, I think, covered in other popular books on astronomy. There is a curious sentence here, though. After describing the ultimate fate of the Sun as a white dwarf, he goes on (page 170): "However, if the star is much more massive than the Sun—at least one and a half times greater mass according to present views—it is believed that the gravitational forces during the collapse are so great that the final state will be that of a neutron star". Black hole *aficionados* (and who is not one nowadays?) will know that if the mass of a star is greater than about one and a half times the mass of the Sun, not only can it not be a neutron star but *sui generis* must become a black hole, unless it sheds some of its mass

As an account of developments in sixteen years of radio astronomy, this book would be a decidedly poor buy (you would still learn more from Graham Smith's excellent old Pelican book). Sir Bernard says that this is not his intention, but why then is there a chapter on cosmology, practically irrelevant to Jodrell Bank's work? Even as an account solely of Jodrell Bank's contribution, the book is unsatisfactory. The performance and capability of the telescopes could have been described, and compared with those at other observatories. A bibliography of Jodrell Bank publications could have been provided (though the referencing is in fact excellent). And I believe space could have been found for all the main research programmes.

The main interest of the book derives, however, from the insight it gives into how a major research establishment is run (a dictatorship, but benevolent, one hopes) and into what goes on at those committee meetings where the taxpayers' millions are carved up.

One remark did intrigue me. After describing experiments in bouncing radar signals off the Moon, Sir Bernard says (page 212): "The system was subsequently widely used for military purposes". Is that to be taken to mean that Jodrell Bank has been used by the military to detect radar signals reflected from the Moon?

M. ROWAN-ROBINSON

Marxist Science

Science and Philosophy in the Soviet Union. By Loren Graham. Pp. ix+584. (Allen Lane: London, September 1973.) £7.

DIALECTICAL materialism is too much like an established religion to be discussed dispassionately. In its name, as in the name of Christianity or of Islam, many terrible crimes have been committed and many errors promulgated. But since any philosophy of science within the Soviet Union is bound to be expressed in the vocabulary of Marx, Engels, Plekhanov and Lenin, it may also take some responsibility for the many valuable scientific discoveries and philosophical insights that have come to some of those gifted people who have sought them honestly within that framework of thought. It is a grave folly to suppose that this particular offshoot of the European philosophical tradition can be dismissed as a farrago of nonsense, on a par with Nazi racism or scientology.

Professor Graham is concerned with the intellectual conjunctions between science and official Marxism in the Soviet Union. Although not in the least a Communist apologist, he explicitly avoids extended discussion of political

his book the Stalinist terror is seen as an irrational brutal fact of life, acting by *force majeure* on a sophisticated but defenceless scientific community. From this (deplorably unmarxist!) viewpoint, the Lysenko affair was a gross aberration, a bizarre and tragic pseudo-scientific interlude of no relevance to the main theme. It is more remarkable that by mixing ideological slogans with subtle technical equivocations the scientific leaders managed fairly well to ward off similar threats to scientific integrity—witness the failure of G. C. Chelintsev's attack on the resonance theory of the chemical bond, and the preservation of quantum theory against a variety of 'philosophical' objections. It could even be argued that Soviet psychology was actually strengthened by the discipline of a strict regimen of Pavlovian conditioning in place of the forbidden ecstasies of the Freudian unconscious.

Anyway, that was all about twenty years ago. Despite many serious disabilities—repression of political dissidence, arthritic administration, obstacles to travel and to the easy flow of information, uneven quality of technical facilities, and so on—Soviet science is very much the same in content as its counterparts in Europe, Japan, India, and the United States. They are under the sway of the same scientific fashions, they take off their hats to the same brilliant performers, and attempt to solve the same scientific problems with the same algebraic formulae, computer printouts, bubble chamber photographs and electron micrographs.

The question is: does the Soviet philosophical commitment to dialectical materialism make a significant difference to Soviet scientific achievements? By an admirable scholarly, intelligent and judicious appraisal of characteristic writings of many leading Russian scientists, Professor Graham provides us with precisely the material we need to make such a judgment for ourselves. He has had to cover a great deal of ground—cosmology, relativity, quantum mechanics, genetics, the origins of life, structural chemistry, cybernetics, physiology and psychology: it is a remarkable achievement to appear so much at ease, so lucid, and so reliable in such a variety of disciplines.

As a practical philosophy of science, dialectical materialism seems to have both strengths and weaknesses. The emphasis on 'materialism', for example, is so close to the naive realism of most active scientists that it contributes very little to our understanding. The attack on philosophical idealism, which was a distinguishing feature of Marxist thought in the late nineteenth century, now looks like flogging a dead horse, and is mainly used now as a form of invective against ideological opponents.

materialism seems to have produced little more than elaborate rationalisations for the acceptability of perfectly respectable scientific concepts such as the relativistic equivalence of mass and energy or the wave-particle duality of quantum mechanics. In the field of psychology this metaphysical commitment merely adds confusion to the undecidable propositions that arise when attempts are made to define consciousness. The swing of fashion in favour of 'cybernetics' (what we now call 'systems analysis', or 'automation') in the Soviet Union in the 1960s suggests that the very word 'materialism' may predispose Russian scientists, philosophers and politicians to the 'technological fix' where more humanistic and humane methods are called for. As Professor Graham remarks "while in the 1930s it was possible to speak of the Bolshevisation of science, in the 1960s it was possible to speak of the scientisation of Bolshevism".

On the other hand, 'dialectics' is a good armour against crude scientism. Dialectical thinking, where the anti-paradigm must always be kept in mind, where the negation of the negation must be envisaged as a higher synthesis, has all the flexibility, subtlety and dynamism of the best creative speculation. In the biological realm, where non-linear cooperative phenomena are primary, the principle of the transformation of quantitative into qualitative differences is particularly valuable as an antidote to naive reductionism. Oparin's brilliant initiative on the origins of life obviously owed a great deal to this way of thought.

But the dialectical process (essentially an abstraction from the real processes of physical tension or of social conflict) is only one of many metaphors that may be applicable to the natural world or to our attempts to describe it. Since the time of Engels—the main authority on dialectical materialism as a philosophy of science—we have learnt to apply other deep and fruitful concepts such as feedback, entropy, complementarity, invariance, symmetry, connectivity, which are equally illuminating. To avail themselves of these powerful concepts many thoughtful Marxists have tried to incorporate them into dialectical materialism by showing that they are somehow subordinate to, or implicit in, the dialectical process itself: in the end, this eclecticism conflicts with the orthodox claim that the philosophy of Marx and Engels was and remains uniquely comprehensive. Official Soviet philosophy will not easily accept that the Marxist categories themselves ought to expand out of recognition, or wither away, under the impact of scientific progress.

A cardinal principle of Marxism has

practice. This principle is mentioned by Professor Graham from time to time, but not, I feel, with adequate critical force. All too often it has been used in Russia as a crude ideological justification of some political or bureaucratic reorganisation *à la* Rothschild, without serious analysis of the underlying problems. A sad feature of the social structure of Soviet science, and of the attitude of Soviet scientists, is the gulf that still exists between the pure and the applied, the academic and the industrial, the basic and the technological. In these respects it is not obvious that the despised and corrupted institutions of capitalism are less 'relevant' than their socialist counterparts. Even within academic research there is a sharper professional distinction, and less intellectual cooperation, between theoretical and experimental physicists in the Soviet Union than in Britain or the USA. One would have more respect for dialectical materialism as a practical philosophy of science if one saw much more of this hypothetical unity in action.

Yet dialectical materialism does have another major virtue: it is a serious philosophy of nature that is genuinely favourable to scientific progress. Within its legitimate spheres, the primacy of scientific knowledge is always to be respected. Any suggestion that there could be a conflict between a scientific discovery and a theoretical deduction from metaphysical foundations is quite foreign to this philosophy, as originally propounded and as now largely practised by Soviet scientists. It is more or less beside the point whether this really means that 'dialectical materialism' is synonymous with the 'scientific viewpoint', or whether it implies no more than that "the Marxist dialectic . . . is a general orientation and culture of thought that helps each person to pose a problem with greater clarity and purpose and thereby helps him to solve the riddles of nature" (N. N. Semenov). As Professor Graham argues, we may reasonably believe Soviet scientists, and accept the evidence of their scientific achievements, when they say that they have been greatly helped in their work by their adherence to this philosophy.

The urge to interpret scientific knowledge within a consistent philosophical framework thus encourages many leading Russian scientists to consider carefully the hidden assumptions and overall structure of their subjects. In our own scientific community the absence of a tradition of serious discussion at this level of generality leaves a gap that is filled by crankiness, amateurish superficialities or ponderous logic chopping. In the Soviet Union, philosophical controversy and polemics within supposedly technical scientific

for a higher degree of general intellectual awareness. What is so depressing is that the political and ideological overtones of such important (and essentially harmless) endeavours repel many thoughtful and intelligent Russian scientists, who try desperately to keep as far away from such matters as they can, and to practise their technical skills even more narrowly than they might in a less wicked world.

All in all, this is evidently a subject of great interest and importance, and we must for long be indebted to Professor Graham for exposing this material to us in such a clear and sympathetic light.

JOHN ZIMAN

Seeing and Believing

Illusion in Nature and Art. Edited by R. L. Gregory and E. H. Gombrich. Pp. 288 (22 plates.) (Duckworth: London, October 1973.) £7.50 cloth; £3.25 paper.

THE reviewer of a symposium is tempted to write another article for the symposium instead of reviewing the articles in it. The six authors who contribute to *Illusion in Nature and Art* omit no essential aspect of the subject, and the examples they discuss are striking. Nevertheless, the temptation has not been wholly resisted.

Two of the articles are not, strictly speaking, about illusion, but about techniques for conveying information about an experience without the perceiver having personally to undergo the experience. Gombrich considers this in the broadest sense. He starts by quoting Plato's condemnation of art as an aspect of the "lower reaches of the soul", and agrees with the diagnosis but not with the condemnation. His article rambles amusingly round the subject and refers often to points made in other articles in the book. He calls attention to Houdon's technical trick for imparting a glint to the eyes in his bust of Voltaire by making a little knob of iris protrude through the cornea. He makes the interesting, and probably valid, assertion that an animal lacking the flexibility and imprecision that enable it to make mistakes could not learn. In a somewhat similar way, Penrose deals with the transmission of information by imprecise means. He stresses that painters and sculptors, like poets, expect the perceiver to do at least half the work. If gross distortion helps, he considers it justified.

The articles by Derogowski and Gregory are more immediately concerned with illusion. Every illustration, whether a line drawing or a minutely executed picture, distorts nature. Seeing it as the representation of something involves framing a



Picasso's *Bull's Head*, made from a bicycle saddle and handlebars, illustrated in *Illusion in Nature and Art* (design and research by Alphabet and Image).

hypothesis to see if it is tenable—as in scientific research. Children, especially those from an environment in which pictures are unknown or unusual, may not immediately comprehend even the most straightforward illustration. Deliberately ambiguous drawings give us an inkling of the nature of the difficulty. Having seen one interpretation it is sometimes difficult to capture the other. Derogowski discusses the effects of culture on this; one tends to select the interpretation that is most compatible with the familiar environment. But there is more to it than that and neither article explores the matter fully.

Escher's drawings are not reproduced in this copiously illustrated book. This is a pity because everyone I have tested sees one of his reversible staircases the same way round at first, then it 'flips' and it is difficult to recapture the first interpretation. What is the basis of immediate, but not lasting, appeal? Drawings of impossible objects, such as the well-known U-shaped trident and Penrose's triangle, are different. They are disconcerting because both forms are seen simultaneously. Blackmore discusses the physiology and neurology of vision and the conditions in which we get contradictory information. He comments interestingly on the role of binocular vision in depth perception: it is useful, but not essential, and is little use beyond about 30 m. At greater distances many other clues can be used though it may take a one-eyed person some time to learn them. A convention in painting is to use blue to emphasise distance. Many painters, from Patinir to Dali, used the technique more impressively than Turner. But it is a fuzzy picture by Turner that is reproduced.

The longest article is by Hinton on camouflage, mimicry and warning in animals and plants. It is packed with information and thoughtful

efficient in the long run that every characteristic is functional. The standard arguments, that the effect of the early steps towards cryptic marking would be too trivial to matter, and that beneficial effects of crypsis have seldom been demonstrated, are countered reasonably enough by the argument that the experiments have been brief and small effects require vast numbers of test organisms. He goes on to argue that a camouflaged organism is seen but not recognised, and that there is no basic distinction between being seen, and rejected as inedible, and being camouflaged. That left me unconvinced.

Eye-spots on butterfly wings probably alarm predators for long enough to permit escape, and they may divert attack to a point less vital than the insect's body. Hinton's suggestion that a chrysalis resembling a monkey's face, and a bug with its head distorted to look like a crocodile, get protection from these resemblances in spite of the difference in size between mimic and model, is intriguing. Insects have a long evolutionary history; it is therefore understandable that effects such as this should be commonest among them. Hinton extends the palaeontological argument by pointing out that a poisonous plant would gain little by using coloured flowers to warn colour-blind herbivorous mammals; he therefore invokes selection during the period when the environment was dominated by lizards with colour vision. Discussing flower colour as an insect lure, he points out that insects see in the ultraviolet; we therefore reach misleading conclusions when we consider the appearance of a flower in visible light only.

The book is handsomely got up and inevitably expensive because of the illustrations. It is a pity that a little more trouble was not taken with it. There are far too many typographical mistakes, some misnumbered pictures and an incompletely labelled graph.

N. W. PIRIE

Water

Water: A Comprehensive Treatise. Edited by Felix Franks. Vol. 2 (Water in Crystalline Hydrates; Aqueous Solutions of Simple Nonelectrolytes). Pp. xix+684. Vol. 3 (Aqueous Solutions of Simple Electrolytes). Pp. xvii+472. (Plenum: New York and London, 1973.) \$43.

In these two volumes Dr Franks has assembled an impressive array of authors and has in the main allowed them complete freedom in dealing with their allocated topics. Since most of them have already made major contributions in their field, the result is a series of expert review articles, some

together provide a mine of valuable information. Everyone working in the field of aqueous solutions should have access to these volumes and they should grace the shelves of most libraries for years to come.

Volume 2 begins with an excellent critical essay, by the editor himself, on the solvent properties of water. Chapters 2 and 3 are concerned respectively with water in stoichiometric hydrates (Falk and Knap) and with clathrates (Davidson). Both these are comprehensive and provide useful background material for an understanding of solutions. Chapter 4 (Luck) is mainly concerned with hydrogen bonding in general rather than with aqueous solutions in particular. Chapter 5 (Franks and Reid) is a valuable and detailed account of the thermodynamic properties of non-electrolyte solutions. This, together with the first two chapters of Volume 3 ("Thermodynamics of Ion Hydration", Friedman and Krishnan; "Thermodynamics of Aqueous Mixed Electrolytes", Anderson and Wood) could form the basis of an excellent text on the thermodynamics of solutions. Volume 2 continues with a factual study on the phase behaviour of aqueous solutions at high pressures (Schneider) and with a group of articles on techniques. Hasted (Chapter 7) contributes a detailed review on dielectric properties with some emphasis on experimental techniques, Blandamer and Fox review spectroscopic properties (Chapter 8) mainly concentrating on ESR evidence, and, in Chapter 9, Blandamer gives a welcome account of a rather less familiar topic, acoustic properties. Zeidler (Chapter 10) deals with NMR studies on aqueous non-electrolytes, and the volume ends with an interesting evaluation of the part played by models in the understanding of water and aqueous solutions (Ben-Naim, Chapter 11). In the course of this, some commonly held beliefs about the interpretation of partial molal heat capacities are drastically undermined.

The first chapter of Volume 3, already mentioned, is an extremely clear and complete account of the thermodynamics of ion hydration, the second a factual study of the application of thermodynamic measurements to mixed aqueous electrolytes. Hepler and Woolley (Chapter 3, "Hydration Effects and Acid-Base Equilibria") discuss the best values of thermodynamic functions for the ionisation of water, and review the reviews on acid-base equilibria. "Ionic Transport in Water and Mixed Aqueous Solutions" (Chapter 4, Kay) describes some modern conductance and transference number equipment particularly suitable for work at high pressures, and reviews work, mainly from his own laboratory, showing how

transport properties. Verrall (Chapter 5) contributes a splendidly critical account of the use of infrared spectroscopy in the study of aqueous electrolyte solutions, the related subject of Raman spectroscopic techniques and their results being entrusted to another author (Lilley, Chapter 6). Herz gives an extended account of the principles of nuclear magnetic relaxation spectroscopy and its applications to electrolyte solutions (Chapter 7). Finally, Pottel extends the theory and practice of dielectric measurements to electrolyte solutions.

No review can do justice to a work which ranges over so wide an area and is written by such authoritative authors. Possibly the editor chose rather too many. There seems little reason, for example, why the main non-thermodynamic techniques should have been cut into sections, one dealing with non-electrolyte, and the other with electrolyte solutions, as in Chapter 7, Volume 2, and Chapter 8, Volume 3. It could be argued that this type of split increases the bulk of the work and makes it more difficult for the reader without gaining anything significant. One should, however, be grateful for large mercies. These volumes with the others in the series will collectively act as a major source of information on almost all conceivable aspects of aqueous chemistry, and, individually, some of the chapters are small masterpieces. One could hardly ask for more.

H. J. V. TYRRELL

Brief Lives

Aldous Huxley: A Biography. Volume 1 1894-1939. By Sybille Bedford. Pp. xv +400 (11 plates). (Chatto and Windus (Collins): London, October 1973.) £3.95.

BIOGRAPHY has clearly established itself as the No. 1 literary art form of the present era. One has only to scan the literary pages of newspapers and periodicals or glance into the windows of booksellers' shops to notice the difference between now and, say, thirty years ago. In establishing itself as the No. 1 literary art form, biography has driven out the novel. The phenomenon is interesting, and to my mind pretty dismaying: it raises a row of interesting questions which have dismaying answers not just for novelists.

To begin with: did biography drive out the novel or was it the novel that abdicated? Then: is biography more in keeping with the general cultural climate of the times; or is the novel in keeping with the artistic climate of the times but the artistic climate itself thought less of? Has the artistic climate hived off from the general cultural climate, falling victim in its separation and remoteness to arcaneity and silliness, to shallowness

I should say yes to all of them, I'm afraid; and cite the turning away of generally-cultured readers from the 'highbrow' novel to 'serious' biography as an illustration. The advent in the novel of what academic critics call Modernism, identifying it at its outset in the work of Henry James and at its apotheosis in that of James Joyce, say a focusing of the novel on "the interior experience". The interior experience is interesting enough; but in the absence of the exterior experience it begins to appear to the generally-cultured reader narrow and sterile and ultimately mindless. When the interior experience is taken to be a *mélange* of sense-apprehensions and instinctive responses, it is indeed mindless.

The novel of the interior experience is by definition not going to incorporate the powerful attention-holding element of narrative, and probably not even the feeble attention-holding element of 'linear thinking'. Biography, on the other hand, has to tell a story, the story of its subject's life. And while giving intimations of his interior experience, it has to trace his exterior experience—a Modern biography that didn't deal with its subject's relation to other people, to society and to external events during his lifetime would seem damned silly. Should one be surprised, then, that the generally-cultured reading public have demoted the Modern and Post-Modern novel, and the novel, *tout court*, from the No. 1 place, and installed biography there?

I was stirred to these thoughts by reading Volume 1, 1894–1939, Sybille Bedford's biography of Aldous Huxley. Mrs Bedford has great literary talent, and through everything she writes shines a sympathetic intelligence—not to say an admirably unforced professionalism as well. Had she, with the present material, written a novel about an Aldous-like character—and she would have done it excellently—it would have been reviewed, along with four or five others, to the tune of about 150 words or less: this biography will be reviewed on its own to the tune of up to 500 words or more. It makes you think.

I should add, of course, that there is currently a revival of interest in Mrs Bedford's subject, including an existentialist campus vogue for his anti-Utopian and disgust-with-life books. In the context of that fashion my own opinions are heretical. When I was an undergraduate I greatly admired *Crome Yellow* and *Antic Hay*: the way he slid intellectual dialogue into the novel was marvellous. I still admire; but re-reading the books, I find they don't wear at all well. There's an air of artificiality, of divorce from the throb of life, which makes them seem thinner, weaker. With hindsight I should say that was what as it became more noticeable and

more obviously characteristic of the author, reduced my admiration for his later books. I regret it. I can see—and Mrs Bedford makes it very plain—that he was a highly intelligent man; a highly erudite man, easily spanning the two cultures (though not much like a scientist); and in a distant, gentle way a very nice man. But the throb of life in him seems to me to have been weak. (One could link that with vulnerability, first to disgust-with-life, and then to escape-from-life into mystical states.)

I go into all this because—another heretical notion—the quality of a biography seems to me to take something from the quality of its subject. The biography of a man in whom the throb of life is weak is likely to have, as it were, lost something before it begins. Furthermore, Mrs Bedford has to cope with most of Aldous's papers having been lost in a fire: it means that an unusual amount of the book is built from what people have told her about him or written to each other about him. That's not necessarily bad—far from it. Gossip, as C. P. Snow has remarked, lies at the heart of novel making—just think of Dostoevski's and Proust's if you doubt it. Mrs Bedford's book has exactly the flavour of close, cosy, penetrating gossip which gives it the immediacy of life. (Incidentally: because so much of the book's material comes from Aldous's wife, Maria, a strong and interesting character, the biography is almost as much hers as Aldous's.)

But I insist that now is not the time to judge the book, when it is only halfway through. Mrs Bedford's primary aim is not to "evaluate" Aldous as a writer, but to draw a portrait of him over the whole of his life; so we simply have to wait to the end. Already one can see her laying the trail, in this volume, of her own perceptions and interpretations to come. But how she will end the book remains to be seen. The story we already know—a sad, sad falling away of a brilliant mind into its own negation: a sad falling away from the outward-looking discipline of rationality to soft, inward-looking experience of hallucinogens. What can she say? It will be fascinating to see.

WILLIAM COOPER

Game of Chance

The Life Game. By Nigel Calder. Pp. 142. (BBC: London, November 1973.) £2.50.

THE theme of this book is evolution: though the author describes a wide range of biological research, it is unified by constant reference to the random events, in the form of mutations and of association of molecules and cells, which are followed by the suitable selection

"The individuals produced by breeding are the various 'plays' or 'moves' of the gene pool which may succeed or fail." Nigel Calder, who also wrote the television programme *The Life Game*, collected much of the information in the book by interviewing the leading researchers in the fields he discusses.

He describes Darwin's theories and neo-Darwinism, and has much to say about Kimura and the neutralist opponents to Darwinism. He then gives an outline of evolution, from hypotheses about natural selection of macromolecules before life began, to Richard Leakey's finding last year in Kenya of a very old and very large human skull which may alter ideas about early *Homo*. The range is wide: Bonner's work on the genetics of nematode worms' nervous systems, Margulis's theories about the bacterial origins of organelles, and the information that geophysics can provide about the separation of the primates in Africa are all discussed. Though the first chapter seems designed more to whet the appetite than to inform systematically, the rest of the book is logically constructed.

No knowledge of biology is assumed. The function of DNA is described adequately without any reference to its chemistry, though a diagram without a legend (page 14) does not enlighten further. Work on spatial information in multicellular organisms is also bravely and quite successfully tackled. An electrophoretic gel is described as an electric racetrack, and the primaeval soup was "about a third as strong in its concentration of organic material as Knorr's Chicken Bouillon".

Although so much detail is left out, the book is very rarely misleading. In some cases it fills gaps left out by conventional genetics textbooks. Thus excellent photographs illustrate the point made that humans cannot be morphologically classified into non-overlapping races. Some confusion between gene loci and alleles seems, however, to have been the origin of the statement that "a brother and sister... differ genetically more than the human species differs from chimpanzees". And although both sides of most arguments are given, Cavalli-Sforza's map of human migration round the world, based on gene frequencies, is offered uncritically with no mention of genetic drift (described later), which many believe makes such reconstructions impossible.

The book is certainly an excellent source of information about modern biology for the layman; but it is so up to date (Maynard Smith's conclusions on animal conflict, *Nature*, 246, 15; 1973, are described) and so wide ranging that most students of biology will find at least an intriguing new morsel of information in it.

GRAHAM MORGAN

CORRESPONDENCE

ERTS

SIR,—It was somewhat enigmatic to find published in your issue of October 19 the somewhat waspish editorial "ERTS: Technological Success, Scientific Failure?" (*Nature*, 245, 345; 1973), together with the research communication "Burning Waste Gas in Oil Fields", by T. A. Croft of Stanford University (*Nature*, 245, 375; 1973).

The former is an ill-considered, unconvincing and poorly argued sermon on scientific and technological priorities. The latter is a dramatic illustration of the potential of imagery produced by high altitude remote sensing techniques for stimulating important economic decisions. In this particular case the profligate waste of non-renewable natural energy resources was revealed across a large area of North Africa and elsewhere. Such observations could only be made by high altitude remote sensing techniques.

While not questioning the undoubted right of your editorialist to his own views on this subject, I would nevertheless have hoped that, in a journal of the stature of *Nature*, editorials would continue to be fair and to present both sides of complex and important issues.

In Canada, the potential economic benefits of remote sensing projects such as ERTS through natural resource assessment, budgeting, and management in such areas as glaciology, hydrology, forestry, limnology, and urban planning, to name but a few, have been recognised by the setting up of a federal interdepartmental agency, the Canada Centre for Remote Sensing (and similar Provincial Agencies), to oversee the work of remote sensing applications.

ERTS has only been in existence for just over a year, during which time a vast amount of very high quality imagery has become available. A major educational effort is needed (and in some places is in process) to provide resource managers, most of whom have been trained in traditional techniques, with the necessary interpretive tools to exploit this new and relatively inexpensive technique to the full.

Satellites are here to stay. Their potential impact on many facets of contemporary applied science and economics is immense.

Yours faithfully,

R. W. NICHOLLS

Professor of Physics,
Director, Centre for Research in
Experimental Space Science,
York University Toronto

SIR,—Thumbs down to your editorial of October 19, "Technological Success, Scientific Failure?" on the Earth Resources Technology Satellite (ERTS). Perhaps you were deliberately being provocative to sting one or two of your readers into clarifying what many are unsure about, in which case, as one of the ERTS principal investigators, I swallow the bait.

Your question is too absolute. From my own field, the mapping of structural and lithological features of the African rift system from ERTS imagery, I can balance your editorial with a criticism of space-viewed geology made by Dr J. V. Hepworth¹ in 1969: "Space photography (and imagery) is a tool *additional* to aerial photography, geological and geophysical mapping, and is not an exclusive source of conclusive answers" (my emphasis). Of course the pressures have been there, as Dr Hepworth noted, to justify the enormous expense of space-viewing by the premature or even invalid seeking of conclusive answers. Ironically, you would now seem to be berating the ERTS project precisely because of its failure to find these answers.

"One cannot imagine why any geologist would be prepared to make a partial map of his area," you say. Yes, and the ERTS imagery shows that all geological maps, on a regional scale at least, have been partial in the sense of our failure to see, on the ground or from aerial photography, all the surface geological data. Despite some grossly exaggerated claims for ERTS, which incidentally have been strongly criticised by NASA scientists themselves², and despite some of the limitations which you yourself mention (for example, the 0930 routine), the imagery provides valuable new scientific information. For the geologist, this has enabled a revision or precision of regional structure, lithological boundaries and even of the geographical base-maps—many river courses and lake shore-lines in eastern Africa, for example, are for the first time known accurately from the ERTS imagery.

Let other scientists speak for other disciplines, but the benefits of ERTS to geology, as of Lunar Orbiters to selenology, are such that one geologist would like to say, "Thank you, NASA."

Yours faithfully,

P. A. MOHR

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¹ Falcon, N. L., Gass, I. G., Girdler, R. W., and Laughton, A. S., *Phil. Trans. R. Soc. A* 267 40 (1970)

² Freden, S. C., and Mercanti, E. P., *Symposium on Significant Results obtained from Earth Resources Technology Satellite-1*; 3 (Discipline summary reports, NASA X-650-73-155, 1973).

Whiter than White

SIR,—Amongst the Short Notes (*Nature*, 245, 404; 1973), the paragraph "Whiter than White" asks if the soap industry has been living in an unreal world because the use of soap per person in Britain has only increased linearly and not exponentially.

Exponential increase is best illustrated in its biological form, where any increase in population is itself capable of reproduction and there is no intrinsic limit to the increase. When increasing areas of the body receive the attention of soap, or rates increase, both areas and frequency of application have finite limits. Similarly, the washing of garments or number of eating utensils used per person must tend to a definite limit and show linear characteristics for a time. I suspect, however, that the data we have are incomplete because a linear increase means that no soap has been used much before 1825.

As a manufacturing company, our interest lies in studying the various opportunities inherent in different growth rates. When the use of a product has a growth rate of only 0.76% per annum, as shown for soap, a proper segmentation of the demand is necessary. By this is meant that specialised demand sectors, such as stainless steel razor blades, enzyme washing powders or nuclear steam boilers can have very large growth rates within an overall small increase in total demand for razor blades, soap or boilers. It is in the early recognition and in the timely development of products for these growth sectors that industries can consolidate, establish or challenge market leadership with the chance of high rewards. As seen from their annual report, Procter and Gamble have made excellent use of their experience in this by a return on capital of over 30%.

May I be permitted to re-phrase your question? Has the scientific community lived in an unreal world for the past hundred years? Can we hope that this evidence of *Nature's* study of annual reports inaugurates a new era of a symbiotic cross fertilisation between industry and science?

Yours faithfully,

W. HILL

Director and Marketing Manager,
Group Headquarters Division,
Clarke Chapman-John Thompson Ltd,
Gateshead Co. Durham NE8 3HS

Paperback Polymorphism

SIR,—D. F. Owen comments (*Nature*, 245, 343) on the variety of colours in which R. A. Fisher's *The Genetical Theory of Natural Selection* is available in paperback, and speculates that Fisher "... would have been delighted to hear that the polymorphism in the paperback edition of his classic work had possibly affected its sales".

I happened to be with Fisher when he opened the parcel containing the first copies of the paperback edition that he had seen: he took one look at the cover (red) and said "Looks like a book by Hogben."

Yours faithfully,

A. W. F. EDWARDS

Gonville and Caius College,
Cambridge CB2 1TA

Announcements

University News

Heriot-Watt University has conferred the title of Professor Emeritus upon Dr Walter G. Green.

The University of St Andrews has appointed Professor Vincent Bruce Proudfoot to the newly established Chair of Geography.

Appointments

Mr Alan V. Holden has been appointed Officer in Charge of the Freshwater Fisheries Laboratory of the Department of Agriculture and Fisheries for Scotland at Pitlochry.

Professor J. Gani, Director of a combined school of the Universities of Sheffield and Manchester, has been appointed Chief of

the CSIRO Division of Mathematical Statistics.

Dr G. F. Humphrey, Officer in Charge of the CSIRO Marine Biochemistry Unit, has been elected Chairman of UNESCO's Intergovernmental Oceanographic Commission.

Miscellaneous

The Zoological Society of London has awarded the first British Zoologist's Medal to Sir Julian Huxley.

A British Society for Population Studies has been set up to continue and expand the scientific study of population questions. The chairman is Professor D. V. Glass of the London School of Economics and Political Science, Houghton Street, Aldwych, London, WC2A 2AE.

The 1973 Soviet State Prizes for science were awarded as follows: to Nikolai A. Borisevich and Viktor G. Vereshchagin for studies of radiation scatter by dispersion systems and the development of a new wide-range infrared filter; to Marat I. Adamovich, Boris B. Govorkov, Anatolii S. Belousov, Andrei I. Lebedev, Sergei P. Kharlamov, Evgenii I. Tamm, Academician Anatolii A. Logunov, Lev D. Solov'ev, Aleksandr M. Baldin and Al'bert N. Tavkhelidze for their work on the photogeneration of π -mesons on nucleons; to Nikolai P. Korneichuk for his work on extremal problems in approximation theory; to Academician Boris P. Nikol'skii, Professor Mikhail M. Shul'ts, Anatolii I. Parfenov, Anatolii A. Belyustin, Vladimir A. Dolidze, Archil N. Khutsishvili, Anatolii S. Benevol'skii, Viktor P. Yukhnovskii, Valentin V. Aleksandrov, Nikolai A. Fedotov and Nikolai A. Izmailov for work on the electrode properties of glasses; to Nikolai G. Rambidi, Yurii S. Ezhov, Petr A.

Akishin, Evgenii Z. Zasorin, Viktor P. Spiridonov and Mikhail I. Vinogradov for developing a new method of high-temperature gas electronography and applying it to study the structure of inorganic molecules at temperatures above 2,500° C; to Aleksei D. Shcheglov, Deputy Minister of Geology of the USSR, for publications on regional metallogeny; to Academician Innokentii P. Gerasimov, Nikolai F. Leont'ev, Yakob G. Mashbin, Dmitrii A. Lillenberg, Feofan F. Davitaya, Vladimir G. Brugger, Anatolii G. Voronov, Aleksandr M. Ryabchikov, and to Antonio Nuñez-Jimenez, Pedro Cañas-Abril, Salvador Massip-y-Valdes and Juan Torrente del Valle for work in compiling the National Atlas of Cuba; to David M. Golub for work on the development of the nervous system and the theoretical and experimental basis for establishing new nerve links and centres; and to Academician Aleksei P. Okladnikov and Viktor I. Shunkov for their five-volume *History of Siberia*.

Solutions to Chess Problems

Problem 1: 1. Q-K2 mate.

Problem 2: 1. Kt-Kt6 mate.

Problem 3: 1. Castles (QR), any; 2. R-Q8 mate. The point of this problem is that Black could have reached the position in the diagram only by moving his king or rook on the immediately preceding move. Thus, although White can legally castle on his own move, Black has forfeited the right to castle on his move (which would otherwise have been a complete resource against the threat of mate).

Problem 4: White's last move must have been K (from K3) x P (Q3) giving discovered check. Black's preceding move to this must have been P (K5) x P e.p. (Q6) giving double check, and White's move before this P (Q2)-Q4. Black's move before this must have been a bishop move to QB4 giving check to the White king on K6. The main 'try' for White's last move in the position in the diagram is K (from Q2)-Q3 giving discovered check, and Black's preceding move being P (QB7) x White piece (QN8)=Kt giving double check. This solution, however, leads to an 'illegal' position as there are too many black pawn captures of white pieces (and pawns) needed to reach it from the pawn formation of the starting position of a game of chess.

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First issue—January 1974

Agricultural Administration

A Quarterly Journal

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and

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*Department of Agriculture, University of Reading, Earley Gate,
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Agricultural Administration provides a high level, critical rather than a 'popular', forum for the interchange of experience in and ideas on administration between different countries, commodities, production systems and social systems. The journal is not concerned with farm management, economics, sociology or policy *per se*, but concentrates on the nature and solution of the administrative problems they create and in particular on the techniques of inducing and administering change by the farmer and consumer in a world where the optimal use of biological resources (including man) may hold the key to survival of this species.

Agriculture in the context of the journal is defined to cover land use (including forestry and recreation), farming, research and extension, rural employment, input supplies and output marketing (including processing), food consumption.

The journal publishes research papers, review articles, case studies and short communications. It also contains reports of conferences and meetings, book reviews and letters to the Editor.

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APPOINTMENTS VACANT

CITY OF BATH EDUCATION COMMITTEE

NEWTON PARK COLLEGE OF EDUCATION

Newton St. Loc, Bath, Somerset, BA2 9BN

Applications are invited for the post of

HEAD OF THE SCIENCE DEPARTMENT

which will become vacant due to retirement on September 1, 1974. The department is large, with excellent facilities, and offers specialist courses in biological and rural sciences to B.Ed. Honours degree level, together with a range of supporting courses. It is hoped that good opportunities will be available to further develop the work of the department in the future. Applicants should have good academic qualifications in one or more of the biological sciences, horticulture, animal science. The appointment will be at Principal Lecturer level, with an allowance at present fixed at £425 per annum.

Further details may be obtained from the Principal at the above address, to whom letters of application (no forms), with the names of three referees, should be returned by December 21, 1973. (1939)

LIVERPOOL POLYTECHNIC School of Pharmacy

PRINCIPAL LECTURER/ SENIOR LECTURER IN PHARMACOLOGY

Applications are invited from graduates in pharmacy, pharmacology, or related fields with specialisation in pharmacology, who have a higher degree together with appropriate academic and research experience.

The person appointed to the Principal Lecturer post will have overall responsibility for the development of undergraduate work in pharmacology and will be expected to promote postgraduate studies and research work.

An appointee to the Senior Lecturer post will contribute to undergraduate and postgraduate teaching and will be expected to engage in research.

Excellent facilities are available and a new animal house is nearing completion.

Salary: Principal Lecturer £3,581-£4,499 p.a.
Senior Lecturer £3,291-£3,928 p.a.

Details available from Staff Office, Department "N", Liverpool Polytechnic, Richmond House, 1 Rumford Place, Liverpool L3 9RH. (1953)

CSIRO

AUSTRALIA

DIVISION OF MECHANICAL ENGINEERING HIGHTT, VIC.

RESEARCH SCIENTIST

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD: SOLAR ENERGY UTILIZATION

GENERAL: For a number of years the Division of Mechanical Engineering has conducted research into the utilisation of solar energy which has achieved international recognition. The facilities available for this research include two field stations located at Townsville, Queensland and Griffith, N.S.W. Both units are sited in areas occupied by other Divisions of CSIRO which are staffed by scientists of various disciplines and in addition, the Townsville site is adjacent to the James Cook University of North Queensland. It is expected that collaborative research programmes will be developed with the Engineering Faculty of this University.

These field stations provide sites and facilities for the establishment of solar energy research programmes under both arid and tropical climatic conditions. These programmes include the operation of experimental equipment to extend theoretical studies and validate computer models of solar energy utilisation systems.

The appointee will be located in Townsville but frequent interstate travel will be necessary.

DUTIES: To study methods of utilising solar energy in the form of heat at low and medium temperatures.

QUALIFICATIONS: A Ph.D. degree in mechanical engineering or equivalent qualifications, and demonstrable research ability. An understanding of computer simulation techniques and field research experience is desirable. Some background in solar energy utilisation would be an advantage, but is not essential.

SALARY: The appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A9,380-\$A14,290 p.a.

TENURE: The appointment will be for a period of three years.

Applications stating full personal and professional details, the names of at least two professional referees and quoting Reference Number 430/326 should reach:

**The Personnel Officer,
Australian Scientific Liaison Office,
64-78, Kingsway, LONDON, WC2B 6BD
by the 18th January, 1974.**

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(2008)

RESEARCH POST

Available shortly to work on problems concerned with developmental control mechanisms under the auspices of the Medical Research Council grant system. Candidates should possess a Ph.D. or have postgraduate research experience. Knowledge of chromatographic techniques and tissue culture an advantage. Salary according to age, qualifications, and experience (commencing salary £2,223 per annum plus superannuation).

Applications, giving full curriculum vitae and the names of two referees, should be sent not later than January 15 to the Administrative Secretary, Strangeways Research Laboratory, Cambridge, from whom further particulars may be obtained. (1927)

MEDICAL RESEARCH COUNCIL

require

ELECTRON-MICROSCOPE LABORATORY TECHNICIAN

Should have experience in processing biological material, thin sectioning and photographic work, and in routine running of an electron-microscope laboratory. Salary for candidates with A.I.M.L.T., H.N.C. or equivalent within range £1,440-£2,292 according to age and experience.

Applications to Dr. H. E. Huxley, F.R.S., Medical Research Council Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH. (2002)



Assistant in Regulatory Affairs Department

Smith Kline & French Laboratories Limited is a major international pharmaceutical company based in Welwyn Garden City. We now require an additional graduate to join our Regulatory Affairs Department, which is the principal interface between the company and the medicines licensing authorities.

The basic requirements are:

a good honours degree in a biological science or pharmacy with, possibly, post-graduate experience in pharmacology.

the ability to present information in coherent, precise reports.

The work will entail the evaluation and editing of data from within the company's own research and from other sources. Experience in the preparation of data for licensing bodies or experience with the requirements of the drug regulatory authorities would be a distinct advantage.

Salaries are competitive and will reflect ability and experience. Conditions of employment are in line with those expected of a large international organisation. Assistance with relocation expenses given where appropriate.

Please write, giving brief relevant details, to:

The Personnel Officer,

(1934)

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VETERINARY GRADUATE

required by Nuffield Institute of Comparative Medicine for 3-year research project on ecology, pathogenesis and immunity in relation to botulism in waterfowl. The work will provide a good research training in veterinary microbiology.

Starting salary from £2,091 to £2,550, according to age and experience; annual increments and F.S.S.U. Curriculum vitae and names of two referees to:

The Establishment Officer,
Zoological Society of London,
Regent's Park, London NW1 4RY.

(1973)

LONDON SCHOOL OF HYGIENE AND
TROPICAL MEDICINE
UNIVERSITY OF LONDON
Keppel Street, WC1

DEPARTMENT OF HUMAN
NUTRITION

Applications are invited for appointment as Lecturer to teach the basic biochemistry of nutrition. Experience and interest in research on protein metabolism would be an advantage.

Salary scale £1,929 to £4,348, with placing according to qualifications and experience, plus a London Allowance of £162. F.S.S.U.

Applications, including full curriculum vitae and naming two referees, should be submitted to the Dean by December 31, 1973.

Further information about the nature of the post can be obtained from Professor J. C. Waterlow at the school. (1975)

Supervisor - Microbiologist

We have a vacancy in our International Development Laboratories for a graduate microbiologist to be responsible for the day to day running of the Analytical Microbiology Section.

The Section carries out large numbers of antibiotic plate assays and tube assays as well as microbial contamination studies and sterility testing. Various automated techniques are employed.

The person appointed will have a B.Sc. or equivalent in Microbiology and at least two years experience of antibiotic assays. Additional experience concerning microbial contamination, sterility testing or statistics would be a distinct advantage. Applicants should also possess good administrative ability and be capable of organising other people.

Excellent working conditions, non-contributory Pension and Life Assurance Scheme. Flexible working hours. 3 weeks 3 days basic holiday.

Apply in writing giving brief relevant details to:



Deputy Personnel Manager,
E. R. SQUIBB & SONS LTD.,
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Moreton, Wirral, Cheshire.

(1975)

SQUIBB

R&D Pharmaceuticals

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To supervise the setting up and operation of a production unit for the extraction of biologically active materials from cultured human cells. The post involves close contact with research workers in both the field of virology and in the development of new tissue culture techniques.

Salary in both instances, will be above average, reflecting the importance of the jobs. Working conditions are excellent, and benefits include contributory pension scheme, first-class staff restaurant, and active sports and social club. Relocation expenses will be taken into consideration.

Please apply to: J. N. Williams,
Assistant Personnel Manager,
G. D. Searle & Co. Ltd., Lane End
Road, High Wycombe, Bucks.,
telephone: High Wycombe 2124.

SEARLE

(2021)

North East London Polytechnic

Department of Applied Biology

Applications are invited for the post of:

Animal House Curator Grade: Senior Technician T5

to be based at our West Ham Precinct, Romford Road, London E15 4LZ. The person appointed will be responsible for the daily running of the Animal House facilities of the Registered Scientific Departments of the Polytechnic under the guidance of the Animal House Management Committee. The suitably qualified candidate will assist in the training of two junior technicians. Experience in administration, animal handling, animal infections and the efficient running of the Cruelty to Animals Act 1876 is essential. Salary on a scale ranging from £2,031 to £2,340 per annum inclusive.

Please request application of the Staffing Office, Romford Road, London E15 4LZ, or telephone 01 555 0811 Ext. 31. Ref. S/CF 124.

For return by 28 December, 1973.

(1994)

UNIVERSITY OF SALFORD

Chair in Geology

Applications are invited for a newly established Chair in the Department of Biology.

Candidates should have had experience in environmental resources in biology, in particular those relating to lakes, rivers and estuaries.

Salary will be at least £5,625 per annum.

Applications, which should contain a curriculum vitae, details of publications and the names of three referees, should be received by the Registrar, University of Salford, Salford M5 4WT, from whom further particulars may be obtained, by December 31, 1973.

(1949)

WESTERN AUSTRALIAN MUSEUM

CURATOR OF FISH DIVISION OF NATURAL SCIENCE

Applications are invited for the above position. Qualifications: A degree in zoology with a higher degree in some aspect of ichthyology or a related field. Preference will be given to applicants with publications in taxonomy and with field experience.

Duties: As Curator of the Department of Fish, to be responsible to the Head of the Division of Natural Science for the development and care of the State collection of fish and research, the conduct of taxonomic research on the collections and the propagation of information about fish to the public. The appointee will be expected to develop a field-collecting programme embracing the marine and fresh water faunas of the State. He will advise and assist the Curator of Display to make displays within his field.

Salary: Curators are employed at Levels 3 and 4, Professional Division (Curatorial Officers), Salaries Agreement 1968. Present salary range Level 3 \$A8,826 to \$A9,708 (by 3 increments), Level 4 \$A9,986 to \$A11,396 (by 3 increments). The appointment will be made within Level 3, promotion to level 4 is consequent upon performance.

Conditions of Salary: Museum staff are employees of the Western Australian Museum under the Museum Act, 1969. Staff are entitled to the same leave and superannuation benefits as are Public Servants employed under the Public Service Act. Other conditions of service are fixed by the Trustees, but are similar to those applying in the public Service. All appointments are subject to confirmation after a probationary period of three months. Salary scales are fixed by arbitration.

Applications: Applications must include information as to nationality, date of birth, particulars of education and degrees. Applicants should also include the names of three referees competent to give information on professional ability and character. The successful applicant will be expected to provide evidence of good health before appointment. A recent photograph would be useful.

Information: Further information on duties and conditions of service may be obtained on application to the Director.

Closing date: Applications will close at Perth with the Director on January 31, 1974.

The Curator of Fish,
Western Australian Museum,
Perth, Western Australia 6000.

(1867)

UNIVERSITY OF LIVERPOOL

DEPARTMENT OF PARASITOLOGY

Applications are invited for the post of LECTURER IN THE DEPARTMENT OF PARASITOLOGY. Candidates should hold a medical qualification registrable in the U.K. or a good science degree and doctorate in relevant subjects. Practical experience in the parasitology of tropical diseases is essential and preference will be given to candidates who already have experience in teaching and/or research on parasitic diseases.

The successful applicant may have the opportunity to spend periods of service on secondment overseas at teaching and/or research centres but will be based in the Department of Parasitology.

The initial salary will be within the range £1,929-£4,989 per annum according to the qualifications and experience of the successful candidate.

Applications, together with the names of three referees, should be received not later than February 28, 1974, by the Registrar, The University, P.O. Box 147, Liverpool L69 3BX, from whom further particulars may be obtained. Quote Ref. RV/N80609.

**PAEDIATRIC RESEARCH UNIT,
GUY'S HOSPITAL MEDICAL SCHOOL**

**SENIOR TECHNICIAN
and TECHNICIAN**

in biochemistry required to work with a team specialising in detection of genetic biochemical disorders. Applicants should be familiar with enzyme assays. Experience in techniques involving microassays and cell cultures would be an advantage. Salary on scales £2,076 to £2,823 or £1,440 to £2,292, plus £126 London Weighting, according to qualifications and experience.

Applications should be sent to the Administrative Secretary, Paediatric Research Unit, Guy's Hospital Medical School, London Bridge, SE1 9RT. (1997)

**NATIONAL UNIVERSITY OF
MALAYSIA
KUALA LUMPUR
NEW SCHOOL OF MEDICINE
APPOINTMENT OF PROFESSORS/
SENIOR LECTURERS**

Malaysia's second medical school has been set up in the National University, in line with the intention of the Government to extend a comprehensive network of centres for health and medical care to the bulk of the population. The school accepted its first students in 1973.

It is now ready to make Faculty appointments, at a level appropriate to a candidate's qualifications and experience, in

**ANATOMY BIOCHEMISTRY PHYSIOLOGY
MICROBIOLOGY PHARMACOLOGY
SOCIAL AND PREVENTIVE MEDICINE
PATHOLOGY** (Histopathology, Haematology, Chemical Pathology)

Salary ranges (£1 sterling equals \$5.68 Malaysian approx.): Professor M\$21,600-M\$27,480 (£3,803-£4,838); Senior Lecturer M\$18,180-M\$21,600 (£3,200-£3,803) per annum, together with Variable Allowance (according to marital status) between M\$150 and M\$400 per month, and Housing Allowance of M\$310 per month.

Appointment would normally be for an initial period of 24 months (extensible).

Further details and information about method of application may be obtained from the Association of Commonwealth Universities (Apts.), 36 Gordon Square, London WC1H 0PF.

Applications close in Kuala Lumpur and London on January 15, 1974. (1993)

**HOUGHTON POULTRY
RESEARCH STATION**

SCIENTIFIC OFFICER

with H.N.C. or an equivalent qualification required for a biochemistry laboratory which provides an analytical service for research on the effects of disease and stress on metabolism.

Candidates should have had experience of automated analytical techniques, trace and mineral element analysis or chromatographic separation methods.

The appointment will be in the Scientific Officer grade within a scale of £1,318 to £2,177 per annum, according to qualifications and experience. Optional superannuation scheme, with an allowance to offset contributions.

Further particulars and application form from the Secretary, Houghton Poultry Research Station, Houghton, Huntingdon PE17 2DA.

Closing date for applications January 14, 1974. (1980)

CSIRO

AUSTRALIA

**DIVISION OF SOILS
TOWNSVILLE, QLD.**

RESEARCH SCIENTIST

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

GENERAL: The Division is concerned with research on soils including pedological, chemical, physical, microbiological, mineralogical and zoological studies, together with the integration of these in investigations of soil fertility and the relationship between plant growth and soil environment. The headquarters of the Division is in Adelaide, with Regional laboratories at Brisbane, Canberra, Hobart, Perth and Townsville. The successful applicant will be located at **Townsville Pastoral Research Laboratory** where a team of soil, plant, and animal scientists are studying basic and applied problems of improved land use in a range of tropical environments. Excellent computing facilities are available, and close liaison is maintained with the James Cook University at Townsville where a chair of Systems Engineering has recently been established.

DUTIES: To conduct field and laboratory research to evaluate the hydrologic parameters necessary for mathematically modelling the effects of various management practices and rainfall run-off relations on major soil landscapes in north-eastern Australia. An attractive opportunity exists for intensive study of existing instrumented catchments on representative sites throughout the region. Experimental study of the effects of different land use practices, e.g. timber clearing, introduction of improved pastures, etc. could be undertaken in co-operation with resident soil, plant and animal scientists.

QUALIFICATIONS: A Ph.D. degree or equivalent qualifications in hydrology, soil physics or engineering, and demonstrable research ability. Some general agronomic or ecological background would be advantageous.

SALARY: The appointment will be made within the ranges of Research Scientist or Senior Research Scientist: \$A9,380-\$A14,290 p.a.

TENURE: Either an indefinite or a fixed term appointment may be negotiated. Indefinite appointments carry Australian Government Superannuation benefits.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting Reference Number 270/434 should reach:

**The Personnel Officer,
Australian Scientific Liaison Office,
64-78, Kingsway, LONDON, WC2B 6BD
by the 18th January, 1974.**

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(2007)

**UNIVERSITY OF LIVERPOOL
DEPARTMENT OF BIOCHEMISTRY
RESEARCH TECHNICIAN**

A Chemist/Biochemist is sought to operate a high pressure liquid chromatograph on a biochemical research project. Experience of chromatography would be an advantage, but is not essential. Candidates should possess a degree, H.N.C. or equivalent. The post is for up to three years in the first instance. Initial salary up to £1,650 per annum, with progression beyond this.

Application forms may be obtained from the Registrar, The University, P.O. Box 147, Liverpool L69 3BX. Closing date 15 JANUARY 1974.

**UNIVERSITY OF READING
DEPARTMENT OF GEOLOGY**

Applications are invited for a **LECTURESHIP IN GEOLOGY**. Candidates will be expected to teach in sedimentology and closely related areas, and to have a major research interest in the chemical and/or biological aspects of this field.

The person appointed should take up duties not later than October 1, 1974.

Further information may be obtained from the Registrar (Room 208, Whiteknights House), The University, Whiteknights, Reading RG6 2AH; by whom applications should be received not later than 15 JANUARY 1974.

Reckitt & Colman

Technician. Neuropharmacology

Reckitt & Colman Pharmaceutical Division is currently undertaking planned expansion of its activity involving expenditure of several million pounds in new facilities. We seek a Technician to join a team of neuropharmacologists investigating the nature of certain mental disorders with a view to developing new methods of treatment:

The successful applicant will be of HNC standard or equivalent in biochemistry/pharmacology and will have experience in the neurochemical techniques used in such investigations.

We offer a competitive salary, first class pension scheme, and other benefits customary in employment by a large British Company.

Please write quoting ref: U.59 to R. A. Sandow, Divisional Personnel Manager, Reckitt & Colman Pharmaceutical Division, Dansom Lane, Hull HU8 7DS.

(2018)



Wellcome

Protein Sequencing

As part of a long-term programme of work on the structure of clinically important proteins, it is intended to appoint a chemist/biochemist in the Department of Protein Chemistry. The person appointed will be responsible to the Head of the Department for determining the primary sequence of proteins. The successful applicant will have had considerable experience of protein sequencing, and should be able to collaborate effectively with scientists in his own and in related disciplines.

Appropriate equipment for the study exists within the Department, and supporting staff are also available.

The post is based at Beckenham, Kent, in pleasant parkland surroundings, near attractive residential areas and yet within easy reach of London. The conditions of employment are excellent.

Applications, giving brief details of background and experience, should be sent to

The Personnel Manager,
THE WELLCOME RESEARCH LABORATORIES,
Langley Court,
Beckenham,
Kent BR3 3BS,
quoting ref. U.427.

(2019)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF CANCER STUDIES

RESEARCH FELLOW

This is a vacancy for a research fellow/associate to carry out a study on the properties of cells derived from tissues treated with carcinogenic agents. The work would involve both tissue culture studies and animal experimentation. The fellowship is supported by the Cancer Research Campaign. Candidates should preferably be postdoctoral but a candidate with a good degree in biological science and experience in the appropriate area would be considered. Salary will be on the scale £1,929-£2,223 for a fellow and £1,569-£2,223 for an associate.

Applications, with curriculum vitae and names of two academic referees, should be sent to Professor D. G. Harnden, Department of Cancer Studies, Medical School, Birmingham B15 2TJ before January 4, 1974: (1921)

**UNIVERSITY OF THE
WITWATERSRAND
JOHANNESBURG
SOUTH AFRICA**

**PRIMATE BEHAVIOUR RESEARCH UNIT
RESEARCH OFFICER OR SENIOR
RESEARCH OFFICER**

Applications are invited for appointment to one of the above posts in the Department of Psychology. Applicants for the post of Research Officer should recently have completed a Ph.D. or be in the process of completing one, and for the post of Senior Research Officer should have a Ph.D. and a good record of published research. The Ph.D. and published research should be in Animal Behaviour, preferably in Primate Behaviour. Applicants for the senior post should state whether they would consider appointment for the junior post. The successful applicant will be expected to engage in full-time behavioural research on primates, to supervise the research of postgraduate students, and to do a limited amount of teaching. Salary will be in the following ranges: Senior Research Officer, R7,245-R9,315; Research Officer, R5,520-R7,935, the initial salary to be determined according to qualifications and experience. Benefits include an annual bonus, pension and medical aid facilities, and a housing subsidy, if eligible.

Intending applicants should obtain the information sheet relating to this post from the Registrar, University of the Witwatersrand, Jan Smuts Avenue, Johannesburg, South Africa, with whom applications should be lodged not later than February 4, 1974. Interested persons in the U.K. may obtain the information sheet relating to this post from the London representative, University of the Witwatersrand (London Office), Chichester House, 278 High Holborn, London WC1V 7HE, with whom a copy of the application should be lodged. (1967)

**UNIVERSITY OF NEW SOUTH WALES
PROFESSOR OF MEDICAL
BIOCHEMISTRY**

Applications are invited for appointment to the second chair to be established in the School of Biochemistry. The other chair is held by Professor E. O. P. Thompson, the present Head of School. Applicants should have appropriate qualifications in medical biochemistry, preferably with a medical degree, and research experience in a related field of biochemistry, with an interest in university teaching and a capability for academic leadership.

The School has extensive undergraduate programmes for students in science, applied science and medicine as well as postgraduate research activities for higher degrees. The professor will supervise and participate in teaching and examining undergraduate and postgraduate students in the School, with particular reference to the training of medical students, and will engage in and promote research and advanced study in the field of his chair. He will be expected to develop a close liaison with the clinical schools and teaching hospitals and may be given an appointment in one or more of the teaching hospitals.

Salary \$A19,102 per annum. Subject to the consent of the University Council, professors may undertake a limited amount of higher consultative work. The University reserves the right to fill any chair by invitation.

For details of appointment, including superannuation, study leave and housing scheme, write to the Association of Commonwealth Universities (Appds.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on

Environmental Pollution and Resources Unit

Scientific Research Administrator

up to £4750

This is an important appointment in the Directorate of Research Requirements, London, which functions as "chief scientist" in the Department of the Environment, advising on the formulation, scale and balance of the Department's total research programme.

The successful candidate will be responsible for defining research requirements in the fields of atmospheric and terrestrial pollution, and of water, bulk minerals and other natural resources.

Candidates, aged at least 28, should normally have a 1st or 2nd class honours degree or

equivalent in Sciences or Engineering and preferably have had experience of research management. Experience in biological work would be an advantage.

Starting salary within the scale £3647-£4750 according to qualification and experience. Promotion prospects. Non-contributory pension scheme.

For full details and an application form (to be returned by 9 January 1974), write to Civil Service Commission, Alencon Link, Basingstoke, Hants, RG21 1JB or telephone BASINGSTOKE 29222 ext 500 or LONDON 01-839 1992 (24 hour answering service). Please quote S/8477/4.

DIRECTORATE OF RESEARCH REQUIREMENTS

(2009)

UNIVERSITY COLLEGE,
GALWAY

LECTURESHIP IN CHEMISTRY

Applications are invited for the above statutory, full-time post. Salary scale £3,450 by £114 (10) to £4,590 per annum, plus family allowances; non-contributory pension scheme. The person appointed will be required to teach and carry out research in inorganic chemistry. The latest date for receipt of applications is January 4, 1974.

Prior to application, further information should be obtained from the Registrar of the College. (1972)

UNIVERSITY OF ZAMBIA

Applications are invited for the following posts in the SCHOOL OF MINES:

1. PROFESSOR/READER/SENIOR LECTURERS/LECTURERS IN DEPARTMENT OF METALLURGY AND MINERAL PROCESSING. Candidates should have a good first degree with specialisation in the fields of Extraction Metallurgy or Mineral Processing. Research or industrial experience would be a further advantage.

2. SENIOR LECTURER/LECTURER IN DEPARTMENT OF GEOLOGY. Candidates should have a good first degree in Geology with subsequent specialisation and a higher degree in the field of Palaeontology and/or Sedimentology.

Appointees will be expected to take up posts by May 1974, but candidates may apply for posts which will arise any time during 1975/76.

Salary scales: Professor K7,400-K7,800 p.a.; Reader K6,800 p.a.; Senior Lecturer K5,600-K6,600 p.a.; Lecturer K4,000-K5,400 p.a. There may be a mines' supplementation in range K500-K2,500 p.a. (£1 sterling=£1.53). The British Government may supplement salaries in range £200-£750 p.a. (sterling) for married appointees or £100-£350 p.a. (sterling) for single appointees (normally free of all tax) and provide children's education allowances and holiday visit passages. Family passages; various allowances; superannuation and medical aid schemes; regular overseas leave.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by air mail, not later than January 14, 1974, to the Registrar, University of Zambia, P.O. Box 2379, Lusaka, Zambia. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (1989)

TECHNICIAN REQUIRED FOR FORENSIC Toxicology Laboratory. Duties will be mainly routine, although the laboratory is actively engaged in research work which will involve the successful applicant. Candidates should have had experience of modern chemical analytical techniques. The post will interest a worker from the medical field.

The post is at present based at Hyde Park Corner, but will move to a modern laboratory complex in Tooting, S.W.17, in April, 1974.

Apply in writing to Mr. J. N. Ramsey, Department of Forensic Medicine, St. George's Hospital Medical School, 9 Knightsbridge, London, S.W.1. (1999)

BRUNEI

AGRONOMIST

Required by the Department of Agriculture to take charge of the Agronomy section and be responsible for an extensive programme of investigations into swamp and rainfed rice, upland crops, tree crops, pastures and horticultural crops. Male candidates only, between 30 and 48 years of age, MUST have a degree in Agronomy, Agricultural Science or equivalent and at least ten years' experience of tropical Agronomy (especially the Humid Tropics).

Commencing salary including inducement allowance will be in the range £2,710 to £4,840 a year according to qualifications and experience. A substantial Gratuity is payable on completion of engagement.

Other benefits include free passages, liberal leave on full salary, outfit allowance, education allowances and Government Quarters at moderate rental.

THERE IS NO PERSONAL INCOME TAX IN BRUNEI AT PRESENT

For further particulars you should apply, giving brief details of experience, to:

crown agents

M Division, 4 Millbank, London SW1P 3JD,
quoting reference number M3F/731108/NF.

(1940)

THE UNITED LIVERPOOL HOSPITALS

Department of Chemical Pathology

SENIOR BIOCHEMIST

Salary: £2,769 per annum to £3,591 per annum.

Applications are invited for the whole-time post of Senior Biochemist.

The Department carries out a comprehensive range of routine and advanced clinical chemistry investigations for the teaching hospitals and for hospitals in the Liverpool Region. There is an associated Metabolic Ward. The Department is recognised for training for the M.R.C.Path. and the M.C.B., and there are excellent opportunities to work for a higher degree.

Application form and job description obtainable from the Acting Secretary, The United Liverpool Hospitals, 80 Rodney Street, Liverpool L1 9AP. Completed forms to be returned by January 5, 1974. (1950)

**ELSEVIER
EXCERPTA MEDICA
NORTH-HOLLAND
ASSOCIATED SCIENTIFIC PUBLISHERS**

wish to appoint a

SCIENTIFIC EDITOR

in the biological sciences for their
subsidiary company
A.S.P. Biological and Medical Press

The successful applicant will probably be between 25 and 30, possess flair and a Ph.D., or at least a good honours degree, in the biological sciences with a specialization in Physiology or Environmental Science.

An additional qualification will be some post university experience that proves organizational and administrative ability, so that the widely diverging and challenging projects that need daily attention will be handled quickly and efficiently.

The job is based in Amsterdam but will involve regular travel abroad.

In addition it offers:

- (i) a wide, developing and challenging career
- (ii) modern working conditions linked to an excellent social service
- (iii) a good salary with additional bonuses.

Applications, which should include a letter explaining why you are suited to this position and a telephone number where you can be reached, should be directed to:

**The Personnel Department
Associated Scientific Publishers
P.O. Box 2400
Amsterdam—The Netherlands
and should arrive by January 1, 1974.**

(1956)

**PLYMOUTH POLYTECHNIC
School of Environmental Sciences**

SENIOR LECTURER/LECTURER II in MINERALOGY

Candidates should have experience in determinative methods and have a wide interest in the applications of mineralogy to environmental and mineral resources studies.

SENIOR LECTURER/LECTURER II in ECOLOGY

Candidates should have interests in quantitative and experimental aspects of Ecology.

Salaries: Senior Lecturer £3,291-£3,655 (Bar)-£3,928
Lecturer II £2,515-£3,243

Details and application forms from the Establishment Officer, Plymouth Polytechnic, Plymouth PL4 8AA, to be returned by January 1.

(1941)

**UNIVERSITY OF DUNDEE
DEPARTMENT OF BIOLOGICAL SCIENCES**

**N.E.R.C.
RESEARCH ASSISTANTSHIP**

(Amended advertisement)

Applications are invited from Botanists or Microbiologists who have at least a second-class Honours degree for a Research Assistantship, to work under the direction of Dr. M. J. Daft on the mycorrhizas in plants colonising coal tips. The appointment is available immediately and will last three years. Starting salary within range £1,230 to £1,450.

Applications, quoting ref. Est./68/73J, and containing the names and addresses of two referees, should be sent as soon as possible to the Secretary, The University, Dundee DD1 4HN, from whom further particulars may be obtained. (1983)

**UNIVERSITY OF MELBOURNE
SENIOR DEMONSTRATORSHIP
in the**

DEPARTMENT OF PHYSIOLOGY

Applications are invited for this position. Qualifications: The applicant should have an Honours Science degree in Physiology, (B.Sc.(Hons.)), a medical degree or equivalent.

Duties: The appointee will participate in the departmental teaching activities, including the organising and supervision of laboratory exercises for undergraduate students. It is anticipated that the appointee's research interests relate to one of the fields being studied at present in the Department. These include: physiology of the mammalian nervous system with emphasis on sensory processes, lipid metabolism and atherosclerosis, cardiovascular, respiratory and renal physiology, haematology and biomedical instrumentation.

Salary: \$A7,270-\$8,698 per annum.

Commencing date: February 1, 1974 or as soon as possible thereafter for one year in first instance.

Further details may be obtained from Professor I. Darian-Smith, Department of Physiology. Applications in duplicate, setting out in full personal details, qualifications and experience, and the names and addresses of three referees and referring to position No. 536-120, should be addressed to The Registrar, University of Melbourne, Parkville 3052, Victoria, Australia.

Applications close on January 7, 1974. (1986)

**NATIONAL INSTITUTE FOR
RESEARCH IN DAIRYING
(UNIVERSITY OF READING)**

Applications are invited for a post of SCIENTIFIC OFFICER in the Bacteriology Department to assist in the Maintenance of the National Collection of Dairy Organisms and in Research in the field of Bacterial Systematics. The work is presently concentrated on the enzymatic and DNA composition of Bacteria. Applicants should preferably have an interest in bacterial physiology and some expertise in biochemical techniques.

An appropriate degree, H.N.D., H.N.C. or equivalent qualification is required. Salary £1,318 to £2,177 with a starting point dependent on qualifications and experience. Superannuation, with an allowance to offset contributions.

Apply on forms obtainable from the Secretary, N.I.R.D., Shinfield, Reading RG2 9AT. Quote reference 73/76. (1834)

**UNIVERSITY OF BRITISH
COLUMBIA**

DEPARTMENT OF CHEMISTRY

Graduate Teaching Assistantships

Graduate Teaching Assistantships are available for candidates with high academic records who wish to pursue further studies towards the M.Sc. and Ph.D. degrees in chemistry. Excellent research facilities are available in all areas of modern chemical science, ranging from bio-inorganic chemistry to chemical physics. Beginning stipends range from \$4,350 to \$4,550 per annum and depend on the qualifications and seniority of the graduate student. In addition, many special merit awards are made to those Graduate Teaching Assistants who show excellence in the performance of their duties. Numerous graduate scholarships are also available for students with outstanding academic records.

Application forms and further particulars may be obtained from the undersigned.

Professor C. A. McDowell,
Department of Chemistry,
University of British Columbia,
Vancouver, British Columbia.

Scientific and Technical Translators

SCIENTISTS able to write good idiomatic English and possessing a very sound reading knowledge of one or more foreign languages are required as freelance translators. Applications are invited particularly from graduates in medicine, pharmacology, chemistry, nutrition, oil refining, physics, all aspects of engineering including electrical and civil engineering, electronics, mining and metallurgy, and printing technology. The main languages of interest are German, French, Italian, Spanish, Dutch, Russian, Swedish, Danish and Norwegian.

Apply in writing, giving full particulars of qualifications and experience and an estimate of weekly output to:

Dr. A. M. A. Mincer, E.T.S., P.O. Box 428, 296 Kingston Road, London SW20 8LZ.

(1955)

UNIVERSITY OF LONDON
KING'S COLLEGE

TEMPORARY LECTURER IN PHYSIOLOGY

Applications are invited for the post of Temporary Lecturer in Physiology, tenable until September 1974. Teaching duties will be particularly directed towards medical students.

Salary up to £3,873 per annum, plus £162 London Allowance.

Further information may be obtained from the Acting Head of Department of Physiology (N), King's College, Strand, London WC2R 2LS, to whom applications should be sent not later than January 2, 1974. (1959)

UNIVERSITY OF WESTERN
AUSTRALIA
PERTH
PHYSICS

Applications are invited for temporary appointment as LECTURER in the Department of Physics. No specific field of interest is associated with this position on which further information is available from the Head of the Department, Dr J. B. Swan, in the University. The appointment will be for 1974 and the appointee will be required to assume duty as early as possible in that year. The salary range is: \$A8,698-\$A11,982 p.a. The appointee will be entitled to appointment expenses of up to \$A1,000.

Applications in duplicate, stating full personal particulars, qualifications, experience and earliest date of availability, should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, by January 12, 1974. Candidates should request three referees to write immediately to the Staffing Officer.

Conditions of appointment obtainable from the Association of Commonwealth Universities (Apts), 36 Gordon Square, London WC1H 0PF. (1991)

UNIVERSITY OF MELBOURNE LECTURESHIP IN THE DEPARTMENT OF HISTORY & PHILOSOPHY OF SCIENCE

Applicants should have professional standing primarily in some historical field of History and Philosophy of Science. Preference will be given to applicants specialising in post-renaissance history of science, other than physics or mathematics. A part of the successful applicant's teaching duties will be to give courses designed for Arts students.

Applications will be considered from persons interested in either a continuing Lectureship or a limited tenure Lectureship of three years, to commence in 1975.

It is hoped that the successful applicant will be able to take up duty by January 1, 1975.

Salary: \$A8,698-\$A11,982.

Further information, including details of application procedure and conditions of appointment for both limited tenure and continuing Lectureships, is available from Association of Commonwealth Universities (Apts), 36 Gordon Square, London WC1H 0PF.

Applications close on February 28, 1974. (1988)

TRENT POLYTECHNIC,
NOTTINGHAM

Principal Lecturer in Research

The Polytechnic seeks to appoint a person who combines a proven ability in research in a specific field or fields with an interest in the co-ordination and management of research across a broad front. Salary scale: £3,581 × £102(4)–£3,989 (Bar) × £102(5)–£4,499 pa.

For further details and form of application, please send self-addressed foolscap envelope to The Chief Administrative Officer, Trent Polytechnic, Burton Street, Nottingham, NG1 4BU. Closing date December 30, 1973.

(1968)

TRENT
POLYTECHNIC

SCIENTIFIC RESEARCH COUNCIL
JAMAICA, W. I.

Scientific Officer

Applications for the post of Scientific Officer in the Mineral Resources Division are invited from suitably qualified persons. The minimum qualifications for the post are:

1. A good degree in Chemical Engineering.
2. Drive, initiative and an interest in research and development. Postgraduate experience either in Industry or in University will be an asset.

Duties will include participation in the Council's projects at the pilot plant stage. Priority attention will be devoted to the processing technology of bauxite.

Salary will be in the range J\$3,480–J\$6,960; the point of entry depending on qualifications and experience.

The Council provides Superannuation, Life and Health Insurance Schemes.

Applications stating age and full details of qualifications and experience together with the names and addresses of three referees should reach the Technical Director, Scientific Research Council, P.O. Box 502, Kingston, Jamaica, W.I. not later than Monday, 31st December, 1973.

(1916)

NEW ZEALAND

Department of Scientific and Industrial Research

Applications are invited for the undermentioned vacancy:

PHYSICAL CHEMIST or MICROBIOLOGIST

The appointee will be based with the team at Taupo, on the shore of Lake Taupo (238 sq. miles in area) in the centre of the North Island of New Zealand.

SALARY: Up to NZ \$9963 p.a. depending on qualifications and experience. Further promotion is on merit. A higher salary may be negotiated for a specially qualified applicant.

DUTIES: DSIR, New Zealand is forming a research team in the Ecology Division to study the causes and effects of the eutrophication of lakes and rivers.

A physical chemist or microbiologist is required to study processes at the sediment/water interface of lakes.

QUALIFICATIONS DESIRED: Ph.D. or equivalent experience in Limnology.

PASSAGES: Fares for the appointee and his wife and family will be paid.

INCIDENTAL EXPENSES: Up to NZ \$120 for a single man and up to NZ \$800 for a married man can be claimed to cover the cost of taking personal effects to New Zealand.

Application forms and general information are available from the High Commissioner for New Zealand, New Zealand House, Haymarket, London SW1Y 4TQ, with whom applications will close on January 18, 1974.

Please quote reference B13/18/130/5947 when enquiring.

(1937)

Editor

John Wiley & Sons
have a vacancy for an Acquisitions Editor
preferably experienced, to take charge of and expand
their publications programme in the life sciences.

A university degree in one of the life sciences is essential and preference will be given to candidates with experience on the editorial side of scientific publishing.

The post is based in Chichester, Sussex, but involves travelling both in this country and abroad. Salary will be according to qualifications and in addition there is a free pension scheme and life insurance. A company car is provided.

• Applications with curriculum vitae and statement of current salary to the
Managing Director
John Wiley & Sons Ltd
Baffins Lane
CHICHESTER
Sussex PO19 1UD

WILEY



(1977)

Immediate vacancy for a fully qualified

technician or graduate

for research work on rheumatoid arthritis, utilising immunological and tissue-culture techniques. Previous experience preferable but not essential.

Apply in writing, stating age and giving details of education, qualifications and experience, to the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT, quoting ref. D.M.2. (1996)

ST. BARTHOLOMEW'S HOSPITAL

PHYSICIST (Basic Grade)

Applications are invited for the post of Physicist in the Radioisotope Department. This is a clinical department which deals with all applications of radioisotopes to medicine. The work involves close co-operation with medical staff in the development of new projects. Opportunities exist for the successful applicant to take the M.Sc. Degree in Radiation Physics. Candidates should have a good honours degree, experience in the field would be an advantage, but is not essential. Salary £1,278-£2,370 plus London Weighting, dependent on qualifications and experience.

Applications to the Clerk to the Governors, St. Bartholomew's Hospital, London; E.C.1, quoting P7/3805/N. (2000)

LA TROBE UNIVERSITY MELBOURNE, AUSTRALIA

CHAIR OF MICROBIOLOGY

Applications are invited for the Chair of Microbiology. This is a Foundation Chair, and the Professor will initially be Chairman of the Department of Microbiology which the University intends to establish within the School of Biological Sciences in 1974.

Microbiology will be offered at undergraduate levels in the School of Biological Sciences in courses for the B.Sc. degree. It is planned that teaching will commence in March 1975. The appointee will be expected to participate in undergraduate and graduate teaching in general microbiology and to carry out research in his chosen field and be responsible for the administration and planning in the department. It is envisaged that teaching should begin at the second-year level. At present the school has departments of biochemistry, botany, genetics and human variation, and zoology.

The date of commencement of the appointment will be by arrangement. Applications close March 15, 1974.

The salary will be \$A19,102 and membership of the University's superannuation scheme is required. Further information and application forms are available from the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF, or from the Registrar, La Trobe University, Bundoora, Victoria, Australia 3083. (1965)

UNIVERSITY OF NOTTINGHAM SCHOOL OF AGRICULTURE

DEPARTMENT OF APPLIED BIOCHEMISTRY AND NUTRITION

Applications are invited from those wishing to undertake research into aspects of the biochemistry and nutrition of amino acids and proteins in animals and to register for a higher degree. Applicants must hold or expect to hold by October 1974 an honours degree or its equivalent in Agriculture, Biochemistry, Chemistry, Nutrition or a related subject.

Applications should be addressed to Professor D. Lewis, Department of Applied Biochemistry and Nutrition, University of Nottingham, School of Agriculture, Sutton Bonington, Loughborough, Leics. LE12 5RD, quoting Ref. 73/123. (1976)

A SCIENTIFIC OFFICER

is required to undertake the design and layout of investigations conducted at the Board's Experimental Station, prepare working documents and subsequently process, analyse and report the data. He or she will also assist in the interpretation of the results obtained from research sponsored by the Board at other research centres and universities.

Applicants should preferably have a degree in Agriculture, Agricultural Science or related biological discipline, with experience in field experimentation and analysis of data. Knowledge of data processing techniques would be advantageous. Salary will be within the scale £2,112 to £2,745 per annum, dependent upon age, qualifications and experience, plus London Allowance of £177 per annum. Pension scheme. Luncheon vouchers.

Application form from Personnel Officer, Potato Marketing Board, 60 Horse Chase, Wellesbourne, Warwickshire CV8 2JF.

GUY'S HOSPITAL MEDICAL SCHOOL

ERGONOMIST

or other Graduate Research Assistant with an interest in biometrics required as soon as possible to join a medical team studying the inter-relationships between work style and back pain.

Further particulars and application forms, to be returned by December 18, 1973, may be obtained from the Secretary, Guy's Hospital Medical School, London Bridge, SE1 9RT.

(2001)

BOARD OF MANAGEMENT FOR
GLASGOW ROYAL INFIRMARY
SCIENTIST FOR MEDICAL
RESEARCH PROJECT

Scientist required for the Centre for Respiratory Investigation, Glasgow Royal Infirmary, to join a multidisciplinary team engaged in the development of new diagnostic tests of lung function based on parameter estimation techniques. In addition to research duties the scientist will be expected to contribute to the continuing development of the routine service provided by the Centre.

Applicants should have an honours degree in electrical engineering or physiology and preferably appropriate experience. The degree could also be in other branches of engineering or in the physical sciences. A postgraduate degree would be an advantage but is not essential. Opportunity to register for a higher degree could be afforded to appropriate candidates. Salary will be according to age and experience in the hospital service and will be in the appropriate Whitley Council Scale for Physiologists/Biochemists. Further information can be obtained from Dr. F. Morgan, Centre for Respiratory Investigation, Glasgow Royal Infirmary. (Telephone No. 041-552 3535, Ext. 278.)

Applications in writing, giving two names for reference, to the Acting Secretary, Board of Management for Glasgow Royal Infirmary and Associated Hospitals, 13 Bath Street, Glasgow G2 1JB, not later than January 1, 1974. (1943)

INSTITUTE OF TERRESTRIAL
ECOLOGY
SCIENTIFIC OFFICER

Salary range £1,318 to £2,177

A Scientific Officer is required by the Institute of Terrestrial Ecology to assist with research on freshwater invertebrates. The officer will be a member of the Wetlands Research Group based in Edinburgh and the work will initially concern the measurement of populations in lakes. Applicants should have some experience in freshwater ecology, particularly zooplankton, and an interest in the management of open waters.

Candidates should be under 27 years of age, with a degree or equivalent in a relevant subject. A current driving licence is essential.

Starting salary may be above the minimum. Superannuation arrangements.

Application forms and further particulars are available from Establishment Division, Natural Environment Research Council, Alhambra House, 27-33 Charing Cross Road, London WC2H 0AX. Closing date January 7, 1974.

NATURAL ENVIRONMENT RESEARCH
COUNCIL.

(1964)

WESTFIELD COLLEGE
UNIVERSITY OF LONDON
Hampstead, NW3 7ST

GRADUATE EXPERIMENTAL OFFICERS required in the Chemistry Department for work in connection with the Circular Dichroism Unit, and the Medical Research Council Steroid Reference Collection. Salary scale £1,679 to £1,939 per annum, according to age and experience.

Please write or telephone to the Personnel Officer (N), Westfield College, Hampstead, NW3 7ST. Tel. 01-435 7141. (1958)

UNIVERSITY COLLEGE HOSPITAL
MEDICAL SCHOOL

GRADUATE RESEARCH ASSISTANT, with good Honours degree, required to join a group studying the effects of abnormal carbohydrate metabolism on the development of vascular complications of diabetes. The assistant will be expected to study for a higher degree. Salary: £1,150 to £50 to £1,250.

Applications in writing, including a curriculum vitae and two references, to Dr H. Heath, Department of Biochemical Pathology, University College Hospital Medical School, University Street, London



Pharmaceuticals
Division

Metabolism Pharmacokinetics

We have vacancies for senior personnel in the Metabolism and Pharmacokinetics Sections of our Safety of Medicines Department.

Major aspects of the research include the investigation of the metabolism of potential drugs and the development of analytical methods for their measurement in biological systems. It is desirable, but not essential, that applicants should have experience in the use of radioisotopes, spectrophotometric, Chromatographic, and other quantitative analytical techniques used in Pharmaceutical Research.

The successful candidates will supervise a group of supporting staff, and will be expected to liaise with chemists, biologists, toxicologists, and clinical research scientists in the development of new drugs.

The research staff at Alderley Park is representative of all scientific disciplines pertaining to research on medical and veterinary drugs. Original and fundamental research is encouraged and much freedom is given to the publication of scientific papers. Conditions of service prospects and the assistance given to married men in moving home are designed to attract and retain staff of this high calibre and would be discussed in detail at interview.

Applications, giving brief details of age, qualifications and experience should be sent to: Miss K. E. Webster, Personnel Department, ICI Pharmaceuticals Division, Alderley House, Alderley Park, Macclesfield, Cheshire.

(1936)



Wellcome

SENIOR TECHNICIAN

This position is in the Department of Drug Metabolism which collaborates with other Departments in the search for and scientific development of new therapeutic agents.

With a considerable background of experience in gas chromatographic techniques and with HNC (Chemistry) or equivalent, the successful candidate will be expected to assist in the co-ordination of the GC section, and to contribute creatively to the solution of biological problems by GC techniques. Knowledge of F & M equipment would be useful and an acquaintance with GC-MS would be a further advantage. Opportunities are available for specialised training and further education.

Our Laboratories are situated in pleasant parkland surroundings within easy reach of Bromley and Beckenham and about 12 miles from Charing Cross.

Please write quoting reference U.426 and giving brief details of qualifications and experience to the Senior Personnel Officer, The Wellcome Research Laboratories, Langley Court, Beckenham, Kent, BR3 3BS. (2020)

An opportunity in

Thrombosis Research

with  **Pharmaceuticals Division**

An opportunity for challenging and interesting research is available at post-doctoral level in the Research Laboratories of the Pharmaceuticals Division of ICI Limited, for a scientist to undertake research in the area of arterial and venous thrombosis.

Independence of thought and originality will be the main requirements for this post. However, previous research experience in this or related areas with particular emphasis on animal models would be an advantage.

The Pharmaceuticals Division is very attractively situated in rural North Cheshire, within easy reach of main road and rail routes. There is a wide range of country and town housing within 20 minutes drive to cater for most tastes. Conditions of service, career opportunities, and assistance given to married men in moving home are designed to attract and retain staff of high calibre.

Applications in writing, giving details of age, qualifications and experience, should be addressed to:

**M F Losse, Personnel Officer,
Imperial Chemical Industries Limited,
Pharmaceuticals Division,
Mereside, Alderley Park, Macclesfield, Cheshire SK104TG**

(2011)

Vegetables Breeder

We are looking for a breeder to continue a programme that has led to some outstandingly successful introductions to national and international trade. The breeder appointed will be suitably qualified and have had some practical post-graduate experience. His/her duties will include breeding and selection of a number of vegetable species, control and maintenance of basic seed, the arrangement of demonstration plots and technical advice to our commercial departments. He/she will join us at a time when we are developing a new breeding station on one of our farms.

The position carries a progressive salary with good fringe benefits and provides an opportunity to work in one of the largest wholesale and retail seed groups in Europe.

Apply:

**Personnel Manager,
HURST GUNSON COOPER TABER LIMITED,
Avenue Road, Witham, Essex.
Tel. No. WITHAM 3451.**

(2013)

UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF BOTANY

Applications are invited from suitably qualified PLANT TAXONOMISTS for appointment as UNIVERSITY LECTURER.

Applications (10 copies), with names of three referees, should be sent by February 10, 1974, to Secretary, Appointments Committee, Faculty of Biology A, Department of Applied Biology, Downing Street, Cambridge CB2 3DX, from whom further particulars may be obtained. (1928)

FIELD STUDIES COUNCIL

TUTOR in Biology at Flatford Mill Field Centre, near Colchester. Single, good degree (botany), and competence in chemistry and physics, interest in quantitative plant ecology an asset. Educational qualification desirable. Research opportunities. Salary £1,101 by £69 to £1,239, plus free board and lodging. Appointment early 1974. Closing date January 1, 1974.

TWO TUTORS in Biology at Orierton Field Centre near Pembroke. Single, good degrees (zoology), one with special interest in terrestrial invertebrate ecology and one in marine biology. Educational qualification desirable. Research opportunities. Salary £1,101 by £69 to £1,239 plus free board and lodging. Appointment early 1974. Closing date January 1, 1974.

Further details and application forms from the Director, Field Studies Council, Preston Montford, Montford Bridge, Shrewsbury SY4 1HW. (1929)

UNIVERSITY OF ABERDEEN

RESEARCH OFFICER IN PHARMACOLOGY

Applications are invited for the above post. Candidates should have a Ph.D. degree or similar qualification and should be interested in neuropharmacology, neurophysiology or neurochemistry. Salary on scale £1,662-£2,304 with appropriate placing.

Further particulars from the Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by January 7, 1974. (1944)

ROYAL POSTGRADUATE MEDICAL SCHOOL

SENIOR TECHNICIAN required in Department of Clinical Cardiology. Qualifications: H.N.C. or equivalent. Salary according to qualifications and experience.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting Reference 2/354/N. (1992)

UNIVERSITY OF BIRMINGHAM

DEPARTMENT OF GENETICS

Applications are invited for the post of **RESEARCH ASSOCIATE** in the Department of Genetics to work on genetic aspects of human behaviour on an M.R.C. supported programme of five years' duration from May 1974. Applicants should have a good honours degree in genetics or psychology with relevant research experience. Salary scale: £1,569-£2,223 (exceptionally £2,718) plus F.S.S.U.

Applications (3 copies), naming 3 referees, by January 11, 1974, to the Assistant Registrar (S), University of Birmingham, P.O. Box 363, Birmingham B15 2TT, from whom further particulars may be obtained. Please quote Ref. NN3. (1969)

ROYAL POSTGRADUATE MEDICAL SCHOOL

STUDENT/JUNIOR TECHNICIAN required in Department of Clinical Pharmacology. Minimum qualifications G.C.E. O-level passes in English, maths and two science subjects. Day release available for further study. Salary according to age and experience.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 20/467/N. (1963)

DEPARTMENT OF BIOLOGY HARVARD UNIVERSITY

For the forthcoming academic year, this department expects to make at least two appointments at the **ASSISTANT PROFESSOR** level. Fields of interest include plant biology, genetics, immunology and developmental biology. The university is an equal opportunity employer; women and members of minority groups are specifically encouraged to apply.

Please have three professional persons write us concerning you, and send your résumé, together with your most significant publications prior to February 15, 1974, to Chairman, Department of Biology, 16 Divinity Avenue, Cambridge, Massachusetts 02138.

EXPERIENCED ELECTRON MICROSCOPE TECHNICIAN required to assist in ultrastructural research in the A.R.C. Unit of Invertebrate Chemistry and Physiology at Cambridge.

Applicants should be experienced in specimen preparation, ultramicrotomy and operation of electron microscope. Previous experience in freeze-etching, cytochemistry or autoradiography would be desirable. Minimum qualifications: H.N.C. or university degree.

The post is established on the University Higher Technician's scale (salary range: £1,926 to £2,436).

Application forms obtainable from the Secretary, Department of Zoology, Downing Street, Cambridge.

Closing date: January 14, 1974. (1951)

MOUNT VERNON HOSPITAL Northwood, Middlesex HA6 2RN

Department of Cancer Research

Applications are invited for the posts of **RESEARCH ASSISTANT** (graduate) and **LABORATORY TECHNICIAN** to assist in karyotype studies on human tumours and premalignant conditions. Experience of chromosome banding and tissue culture techniques would be an advantage.

Salaries in accordance with qualifications and experience (Universities and Whitley Council scales respectively).

Please reply to Secretary, Department of Cancer Research (tel. Northwood 26111, extension 258). (1948)

UNIVERSITY OF THE WEST INDIES JAMAICA

Applications are invited for (a) **LECTURESHIP** or (b) **ASSISTANT LECTURESHIP** in **DEPARTMENT OF CHEMISTRY**. Candidates with specialisation in any branch of chemistry may apply. Appointee is expected to have major responsibility in the Freshman year courses. Salary scales (under review): (a) £1,850-£3,265 per annum, (b) £1,500-£1,660 per annum. Child allowance. F.S.S.U. Family passages; triennial study leave.

Detailed applications (6 copies), including a curriculum vitae and naming 3 referees, should be sent by airmail as soon as possible to the Registrar, University of the West Indies, Mona, Kingston 7, Jamaica, West Indies, from whom particulars are obtainable. (2022)

THE UNIVERSITY OF SHEFFIELD EXPERIMENTAL OFFICER

Applications are invited for a post of **Experimental Officer** to operate and maintain a Fourier-Transform N.M.R. Spectrometer in the Department of Chemistry. The successful applicant, who should be a graduate or have an equivalent professional qualification, will be responsible for operating a service in connection with a number of research projects in inorganic, organic, and physical chemistry. Previous experience in one or more of the following fields would be an advantage, although not essential: N.M.R. spectrometry, chemical instrumentation, electronics, and computing. The post is financed by the Science Research Council and the starting salary will be in the range £1,596 to £2,088 plus superannuation benefit.

Applications, including details of previous experience and the names of two referees, should be sent to Professor P. M. Maitlis, Department of Chemistry, The University, Sheffield S3 7HF, from whom further particulars may also be obtained. Quote Ref. R4/G. (1865)

UNIVERSITY OF BIRMINGHAM DEPARTMENT OF ANATOMY

A vacancy exists for a **TECHNICIAN** to assist in research on the differentiation of skeletal muscle. The appointee's duties will include the preparation of miniature electronic implants, and the provision of assistance in aseptic surgical procedures and in the acquisition and analysis of experimental data. Opportunities exist for participating in the application of new electronic techniques in these experiments.

The post is suitable for an applicant with an appropriate scientific qualification who is interested in acquiring experience in biomedical engineering techniques.

Salary £1,650 to £1,920 per annum.

Applications to Assistant Secretary (Personnel), University of Birmingham, P.O. Box 363, Birmingham B15 2TT, quoting reference 401/B/979. (2005)

PHYSICIST REQUIRED FOR VACANCY in small M.R.C. team working on the development and behaviour of the avian embryo, including its capacity to receive and transmit signals. We want a research worker who will make use of his basic knowledge to help solve our problems. Some aptitude for electronics essential. Medical Research Council scales. F.S.S.U.—Inquiries to Margaret A. Vince, Psychological Laboratory, Downing Street.



**Public Service
Canada**

**Fonction publique
Canada**

THIS COMPETITION IS OPEN TO BOTH MEN AND WOMEN

RESEARCH SCIENTIST

Salary to \$24,262

**Institute of Sedimentary and Petroleum Geology,
Geological Survey of Canada,
Department of Energy, Mines and Resources, Calgary, Alberta**

DUTIES: Under the general direction of the Head of Micropaleontology Section, Paleontology Subdivision, the Micropaleontologist will carry out independent and team research projects using foraminifera and other microfossils from the Mesozoic rocks of the Arctic Islands and parts of the northern mainland. Establish and apply models of the biostratigraphic framework and paleoecological environments, as well as establishing local, regional and world-wide correlation. The research will be based on outcrop stratigraphic sections and on well material; and will include field studies in arctic Canada. Objectives include publications describing biostratigraphic zonation and monographing foraminiferal and other associated microfossils.

QUALIFICATIONS: Include a doctorate degree, or a lesser degree with a combination of training and research experience equivalent to that required for a doctorate degree, in a discipline related to the duties of the position and extensive experience in biostratigraphical studies of Mesozoic sequences.

Knowledge of the English language is essential for this position.

Forward "Application for Employment" (Form PSC 367-401), available at Post Offices, Canada Manpower Centres, Public Service Commission of Canada offices, or detailed résumés before January 30, 1973, to:

**Sciences and Technology Program,
Public Service Commission of Canada,
Ottawa, Ontario K1A 0M7.**

Please quote reference number 73-110-63 in all correspondence.

Appointments as a result of this competition are subject to the provisions of the Public Service Employment Act. (1931)

Research Microbiologist

We are seeking the services of a Post-doctoral Microbiologist to join our Cell Biology Unit at Welwyn Garden City. The Unit based in recently completed buildings where facilities and working conditions are excellent. The successful candidate will join an active group conducting original research into a variety of microbiological problems, will be expected to make a positive contribution towards innovation in these and related fields and will report directly to the head of the Unit. Experience of antimicrobial testing and the use of laboratory scale fermentation facilities will be of advantage.

The person appointed will probably be in the age range 25 to 30 and should preferably have had some post-doctoral experience.

For an application form and further information please apply in writing, quoting Reference RH5, to the Senior Welwyn Personnel Officer at the following address.



**Roche Products Limited
Welwyn Garden City Hertfordshire AL7 3AY**

(1926)

Universiteit van Amsterdam

The department of Physiology, Faculty of Medicine, has an opening for a

software specialist



for the development of system software and application programs for its PDP-11/40 computer, which will be installed early 1974.

This computer will be used for physiological/biophysical research (control of experiments, signal analysis, data reduction, etc.) under real time multiprogramming monitor (RSX 11-D).

Applicants are required to be thoroughly experienced in machine-language programming.

In addition, they are expected to have an academic education, e.g., in applied mathematics, biophysics or physiology.

Please send application, including a curriculum vitae, to Professor J. Th. F. Boeles, Fysiologisch Laboratorium, Jan Swammerdam Instituut, 1e Const. Huygensstraat 20, Amsterdam, the Netherlands.

Information can also be obtained by telephone (020-181313, extension 80).

(2014)

LECTURER IN METEOROLOGY

South Africa

A Senior Meteorologist is required by the Weather Bureau in Pretoria to undertake full-time lecturing in meteorology at the University of Pretoria.

The University runs an introductory course in general meteorology, followed by courses in dynamical meteorology, numerical forecasting, physical climatology, cloud physics and Physical meteorology, during the 2nd to 4 years of its 4-year B.Sc. (Meteorology) course. The successful applicant will be assisted by part-time lecturers from the Weather Bureau.

Applicants should possess an appropriate M.Sc. or higher degree in meteorology and any teaching experience will be taken into account.

Salary will depend on qualifications and experience, but will be in the scale R5700 x R300-R6900 (£1=R1.63 approx.) plus 15%.

Please apply to the Civil Service Officer, South African Embassy, Trafalgar Square, London WC2N 5DP.

(1932)

ROYAL POSTGRADUATE MEDICAL SCHOOL

SENIOR TECHNICIAN

required in Department of Haematology. Opportunity is available to study for the special exam in Blood Transfusion. Starting salary and grading according to qualifications and experience.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, DuCane Road, London W12 0HS, quoting reference 7/106/N. (2017)

THE ROYAL VETERINARY COLLEGE

UNIVERSITY OF LONDON

BIOCHEMISTRY TECHNICIAN (University Grade 3) required to assist in research and teaching laboratories.

Salary on scale, rising to £2,095 per annum, inclusive.

The work includes assistance with research on isolated enzyme systems and previous relevant experience would be advantageous.

We would consider the appointment of a trainee (age 16-21), in which case the salary would initially be on the trainee scale, rising to £1,426 per annum.

Please apply, giving full details of age, qualifications and experience, to Miss J. Irons (N), The Royal Veterinary College, Royal College Street, London NW1 0TU (telephone 01-387 2898). (2016)

CHELSEA COLLEGE

UNIVERSITY OF LONDON

LABORATORY TECHNICIAN (Grade 2B) required to assist in the general preparation for B.Sc. Microbiology classes and the routine maintenance of Microbial cultures. Salary scale £1,699 to £1,969 per annum (including London Allowance).

Application forms from Mr K. C. Harris, Department of Applied Biology, Hortensia Road, London SW10 0QX. (2012)

UNIVERSITY OF BRISTOL

DEPARTMENT OF PHYSICS

RESEARCH ASSISTANTSHIP IN GLACIOLOGY: on a project to measure the growth or decay of the Antarctic ice sheet by using a radio echo technique. Applicants should be graduates with a good knowledge of physics; field work would be optional. Starting salary up to £2,388 per annum.

Curriculum vitae and the names and addresses of two referees to Professor J. F. Nye, H. H. Wills Physics Laboratory, Tyndall Avenue, Bristol BS8 1TL. (1970)

DEPARTMENT OF NEUROLOGY

ROYAL FREE HOSPITAL

Applications are invited for the post of **JUNIOR TECHNICIAN** to assist in research in the electron microscope laboratory. Opportunities for further study are available. Salary £708 to £1,395 per annum.

Applications, with names of two referees, should be submitted to Personnel Department, 21 Pond Street, London NW3 2PN. Telephone: 01-794 0431. (1933)

UNIVERSITY OF LONDON

CHAIR OF GEOLOGY AT QUEEN MARY COLLEGE

The Senate invite applications for the above Chair, vacant from October 1, 1974. Salary not less than £5,625 per annum, plus £162 London Allowance.

Applications (10 copies) should be received not later than February 1, 1974, by the Academic Registrar (N), University of London, WC1E 7HU, from whom further particulars may be obtained. (1961)

RESEARCH ASSISTANT REQUIRED BY INSTITUTE OF CANCER RESEARCH, Belmont, Sutton, Surrey, to join team studying immunotherapy of human acute leukaemia. The candidate will be required to measure by *in vitro* techniques, the immunological response of patients to leukaemia cells. Experience in tissue culture essential and experience in immunological techniques desirable. Salary according to experience, in Senior Technician scale, currently, £2,202-£2,949 per annum.—Please apply in duplicate to the Secretary, Institute of Cancer Research, 34 Sumner Place, London, S.W.7, giving the names and addresses of two referees and quoting Ref. No. 301/B/494. (1938)

SECRETARY. Graduate required as Personal Assistant to the Director of Research and Managing Director. Shorthand or audio-typing essential. An interest and some basic training in scientific/medical subjects essential. Company engaged in drug research. Very interesting work and excellent conditions, with pension and assurance scheme in operation.

Apply BIOREX Laboratories Ltd., Biorex House, Canonbury Villas, London N1 2HB.

(1974)



Scientific Sub-Editor

To control accuracy of data in new computer system for agricultural information services and to assist with future development work.

QUALIFICATIONS: Experience and/or qualifications in Agriculture or Biology. Familiarity with bibliographic or editing work an advantage.

SALARY: According to experience, in the range £1,318-£1,992 (bar)-£2,667. Pension under F.S.S.U., with an allowance of 4½% salary to cover personal contributions.

Further details and application forms (to be returned not later than January 21, 1974) obtainable from the address below, which is also the location of Systems Group, CAB.

**The Secretary,
Commonwealth Agricultural Bureaux,
Farnham House, Farnham Royal, Slough SL2 3BN.
Tel. No. Farnham Common 2281.**

(2015)

SCIENCE GRADUATE

required for technical post in the heart/lung, intensive therapy unit and anaesthetic research unit of The London Hospital (Whitechapel).

The post will be both technical and scientific and will involve clinical measurement, blood gas analysis, gas analysis and the operation of heart/lung equipment, i.e., pump, transducers monitoring equipment and hyperthermia equipment.

Applications to R. C. Taylor, Assistant Secretary, The London Hospital (Whitechapel), Whitechapel, London E1 1BB. Tel. 01-247 5454, ext. 388. (1966)

UNIVERSITY OF ABERDEEN RESEARCH ASSISTANT DEPARTMENT OF MEDICINE

Applications are invited for a Graduate with a good honours degree in Biochemistry to participate in a study on blood coagulation, with particular reference to haemophilia. Post is for two years and is supported by a Scottish Home and Health Department grant. Salary in range £1,509-£1,734.

Further particulars from The Secretary, The University, Aberdeen, with whom applications (2 copies) should be lodged by December 20, 1973. (1978)

LECTURES AND COURSES

THE CITY UNIVERSITY

DEPARTMENT OF CHEMISTRY

A course of postgraduate lectures on "Explosions: Nature, Effects and Protection", arranged by Professor J. H. Burgoyne, will be given from February 18 to 20, 1974.

Further details may be obtained from The Head of the Chemistry Department, The City University, St. John Street, London EC1V 4PB.

(1946)

UNIVERSITY COLLEGE LONDON

The college will again offer a one-year advanced course leading to the University of London

M.S.C. IN CONSERVATION

Applicants will normally be expected to have obtained a first- or second-class honours degree in Agriculture, Biology, Botany, Forestry, Geography, Geology, Zoology or other appropriate subjects. The course is constantly adjusted to new needs in conservation and is recognised for the tenure of N.E.R.C. Advanced Course Studentships.

The course begins in September 1974 and runs for one calendar year. Closing date for applications January 15. Particulars and application forms from Registrar, University College London, WC1E 6BT. (1962)

FELLOWSHIPS AND STUDENTSHIPS

SALTERS' INSTITUTE OF INDUSTRIAL CHEMISTRY FELLOWSHIPS

Applications are invited for SALTERS' FELLOWSHIPS, of value in the range £2,350 to £2,500, according to qualifications and experience (plus cost of living allowance when held abroad and 10 per cent as contribution to F.S.S.U.).

These Fellowships may be held by Honours graduates, or holders of equivalent qualifications, in chemistry, chemical engineering or other branches of engineering, biochemistry or physics, who desire to obtain further training in research in chemistry, chemical engineering, chemical technology or biochemistry.

Candidates should have obtained a doctor's degree or have had not less than three years' postgraduate experience by the time of their taking up the Fellowship. A high standard will be required.

Generally Fellowships will be tenable for one year from September 1, 1974, and may be renewed for one further year.

Applications should be received by the Clerk of the Salters' Company, 36 Portland Place, London W1N 4DL, by January 21 1974. Forms of application may be had on request.

Applications may also be made at any time during the year, but such late applications will only receive consideration if there are vacancies. Intending applicants for 1975/76, who propose to spend an intervening year abroad, may complete forms of application now. These should be returned by January 21, 1974.

No applicant can be appointed without interview. (1979)

DEPARTMENT OF EDUCATION DUBLIN

POST-DOCTORAL RESEARCH FELLOWSHIPS

Applications are invited for Research Fellowships in Science (excluding Medical and Social Science) and Engineering tenable in any one of the following institutions in Ireland: University College, Dublin; University College, Cork; University College, Galway; Trinity College, Dublin; An Foras Taluntais (The Agricultural Institute); the Institute for Industrial Research and Standards.

Fellowships, up to 12 of which may be awarded, will be tenable for a period of two years, with the possibility of an extension for a third year. Applicants should hold the degree of Ph.D. or have equivalent research experience. Applications will be considered from engineers or technologists with suitable industrial experience. Candidates should not be more than 30 years of age but, preferably, they should be under 28 years of age. Appointments will be effective from a date not earlier than October 1, 1974. The initial salary, which will depend upon qualifications and experience, will normally be within the range of £1,907 to £2,202 per annum, but awards of up to £2,620 may be made in the case of engineers and technologists whose industrial experience or other special circumstances warrant it.

Full particulars of the scheme, including application forms, may be obtained from the Secretary, Department of Education (Headquarters Section), Marlboro' Street, Dublin 1, to whom applications for Fellowships should be forwarded. The latest date for the receipt of applications is February 11, 1974. (1945)

THE QUEEN'S UNIVERSITY OF BELFAST Northern Ireland

DEPARTMENTS OF BIOCHEMISTRY AND MEDICINE

POST-DOCTORAL RESEARCH FELLOWSHIP

Applications are invited for an M.R.C.-sponsored Post-doctoral Research Fellowship to collaborate with Dr R. F. Murphy, Dr K. D. Buchanan and Professor D. T. Elmore on the chemical and physiological characterisation of polypeptides from gut which have immunoreactive properties similar to glucagon. radioimmunoassays and affinity chromatography are routinely used in this work. Applicants should have experience in protein chemistry.

The appointment is for three years, with a salary of £1,929 to £2,058 to £2,223, plus F.S.S.U. Further particulars and application forms may be obtained from any of the above, c/o Department of Biochemistry, Medical Biology Centre, The Queen's University of Belfast, Belfast BT9 7BL. (1984)

European Molecular Biology Organization (EMBO)

Short- and long-term fellowships in molecular biology

The European Molecular Biology Organization intends to award to scientists working in laboratories within the European area both short-term (from a few days to several weeks) and longer-term fellowships for collaborative research or advanced training in molecular biology.

The Short-term Fellowships are to support visits to other laboratories for the purpose of carrying out experiments with special techniques or of other forms of scientific collaboration or advanced training, and especially to support developments arising at short notice.

The Long-term Fellowships will usually be for a period of one year, but applications for renewal will be considered. They will be awarded upon individual application, at the "junior" level to promising young research workers who may then spend prolonged periods in other laboratories working under the guidance of leaders in the field of molecular biology. At the "senior" level, they may be awarded to enable established research workers to gain experience in new approaches and new problems. Upon application by European Institutions fellowships at the "senior" level may also be awarded to specialists who can assist in the initiation and development of research programmes in the sponsoring Institution. Such "sponsored" awards may be made to established workers at all stages of their career beyond the postdoctoral stage.

Application forms and further details may be obtained from Dr. J. Tooze, Executive Secretary, European Molecular Biology Organization, 6900 Heidelberg 1, Postfach 2029 (Postfach 1022.40 after July 1, 1974), Germany.

Application for Short-term Fellowships may be made at any time and will be decided upon soon after receipt of the application. Applications for Long-term Fellowships should be made before February 1 for a decision by April 30 and before August 1 for a decision before October 31. Because the selection procedure involves an interview these deadlines for application should be respected.

(X1822)

UNIVERSITY OF OXFORD TURNER AND NEWALL RESEARCH FELLOWSHIP

Applications are invited for the above post, tenable from October 1974 for two years. The Fellowship is for post-doctoral research in Chemistry, Physics, Geology, Mineralogy, Metallurgy, Applied Mathematics, Engineering or related technologies.

Details may be obtained from the Secretary of the Committee for Turner and Newall Fellowships, University Registry, Broad Street, Oxford OX1 3BD, to whom applications (six typed copies) should be sent by January 8, 1974. (2010)

UNIVERSITY OF LIVERPOOL FELLOWSHIPS IN NUCLEAR PHYSICS

Applications are invited for Research Fellowships in Nuclear Physics tenable in the Department of Physics. Candidates should be Ph.D. standard, with special aptitude for research in high energy physics or nuclear structure physics. The Fellowships are tenable year by year for not more than three years at a salary in the range of £1,929-£2,223 per annum, together with F.S.S.U. benefits.

Applications, three copies, stating age, details of qualifications and experience, publications, research work in progress and completed, together with the names of two referees, should be received not later than February 28, 1974, by the Registrar, The University, P.O. Box 147, Liverpool L69 3BX, from whom further particulars may be obtained. (Candidates overseas who find it more convenient to do so may send one copy only by airmail. Quote Ref. RV/N/80608. (1998)

UNIVERSITY OF SURREY Applications are invited for appointment as RESEARCH FELLOW

in the Measurement Science Laboratory of the Department of Chemical Physics to assist in the development of a new method for the measurement of multiphoton network scattering parameters from 1 MHz to 1 GHz. A detailed knowledge of S parameters is not essential, but a sound knowledge of linear circuit theory and design as applied to coaxial measurement systems is necessary. The appointment is supported by a three-year S.R.C. grant in the salary range £1,929-£3,048. The starting salary will be governed by qualifications and experience. Applicants must have a Ph.D. or equivalent qualifications with several years' experience in a research or development environment.

Applications should be sent to Professor D. Woods, University of Surrey, Guildford, Surrey, giving full details of age, education, qualifications, experience, any published papers together with the names of two referees. (1995)

UNIVERSITY OF RHODESIA INSTITUTE OF MINING RESEARCH RESEARCH FELLOWSHIP OR JUNIOR RESEARCH FELLOWSHIP

Applications are invited for a Research Fellowship or Junior Research Fellowship in the Institute of Mining Research at the University of Rhodesia.

The candidate will be required to carry out research on the distribution and chemical and physical characteristics of coal in Rhodesia. This geological and geochemical study will complement the Institute's research programme in ferrous pyrometallurgy, and special attention will be given to the distributions of the elements, sulphur and phosphorus. The investigation has a particularly wide scope and it offers an unusually good opportunity for geological research directly related to important industrial problems.

The successful applicant will have a good honours degree in geology, and preferably some industrial experience in coal geology.

The appointee will be able to apply to register the project for a higher degree of the University of Rhodesia.

The Fellowship is for a period of two years, but, subject to satisfactory progress, is renewable for a third year.

Salary scale (approximate sterling equivalent): Research Fellow Grade II, £2,511 by £130 to £3,031; Junior Research Fellow, £1,992 by £130 to £2,382. Starting point depending on qualifications and experience. Superannuation and medical aid schemes. Small housing allowance.

Applications (six copies), quoting Ref. No. UK/30, stating where advertisement seen, and giving full particulars, including full names, place and date of birth, telephone number, etc., qualifications and experience and naming three referees, should be submitted by December 31, 1973, to the Assistant Registrar (Science), University of Rhodesia, P.O. Box MP 167, Mount Pleasant, Salisbury, Rhodesia. Additional copy to the Association of Commonwealth Universities (Appts.), 36 Gordon Square, London WC1H 0PF, from whom further information may be obtained. (1960)

UNIVERSITY OF CAMBRIDGE DEPARTMENT OF PHYSICS

Two Research Studentships are available from early 1974 for studies, leading to the Ph.D. degree, of (1) the effect of surface coatings on the impact and abrasive resistance of materials; (2) the reactivity of solids.

Candidates, who should have first or upper second degrees in Physics, Materials Science, or Physical Chemistry, should write to the Secretary, Cavendish Laboratory, Madingley Road, Cambridge CB3 0HE. (1947)

THE QUEEN'S UNIVERSITY OF BELFAST

RESEARCH STUDENTSHIP IN ORGANIC CHEMISTRY

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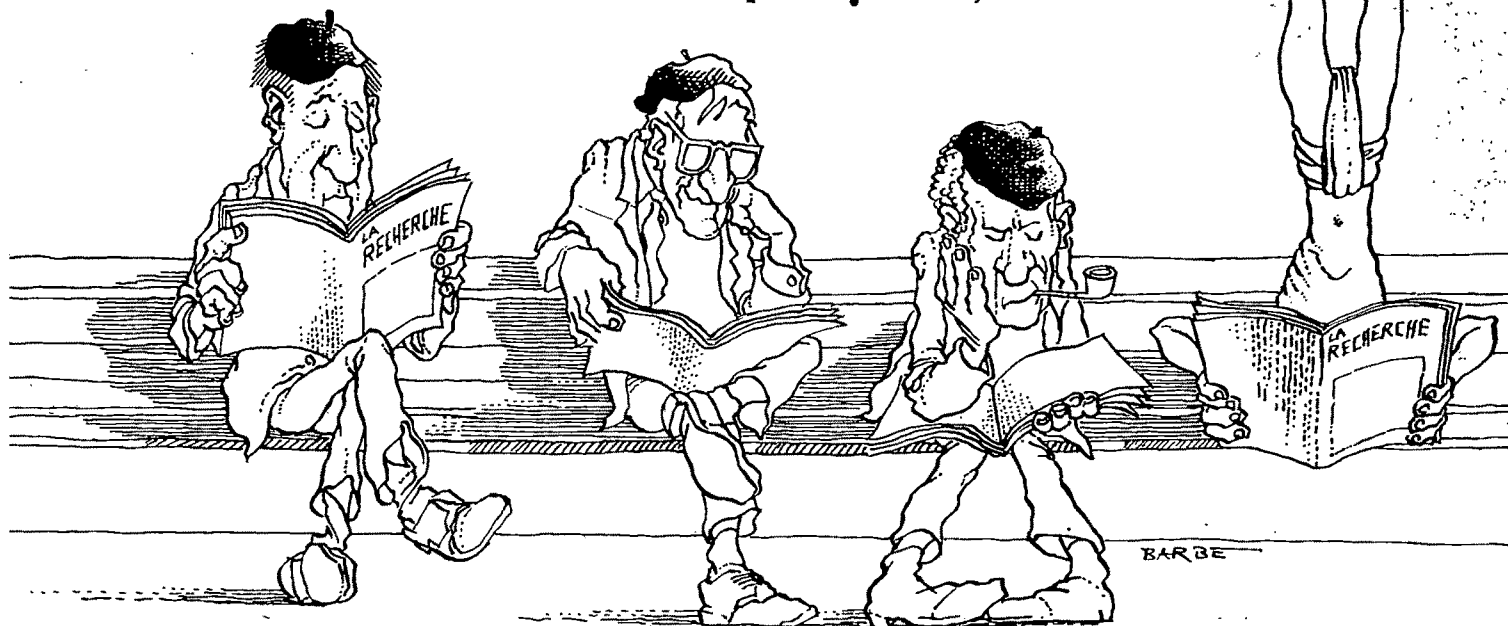
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the candidate wishes to pursue his research (except in the case of London University, where enquiries should be directed to the Academic Registrar), and must be returned duly completed by 8th January, 1974. Candidates desiring to work in Europe (and only those candidates) should apply to Dr. T. I. Williams, Research and Development Department (Academic Liaison), Imperial Chemical House, Millbank, London, SW1P 3JF. Candidates need apply to only one university, but may apply to not more than three if they so wish. In the case of multiple applications, separate forms must be completed in respect of each university. Among other information, candidates will be required to submit a brief *curriculum vitae*, a clear summary of the research programme proposed, and the names of two referees. Other things being equal, preference will be given to candidates proposing to carry out their research at institutions other than that from which they make application.

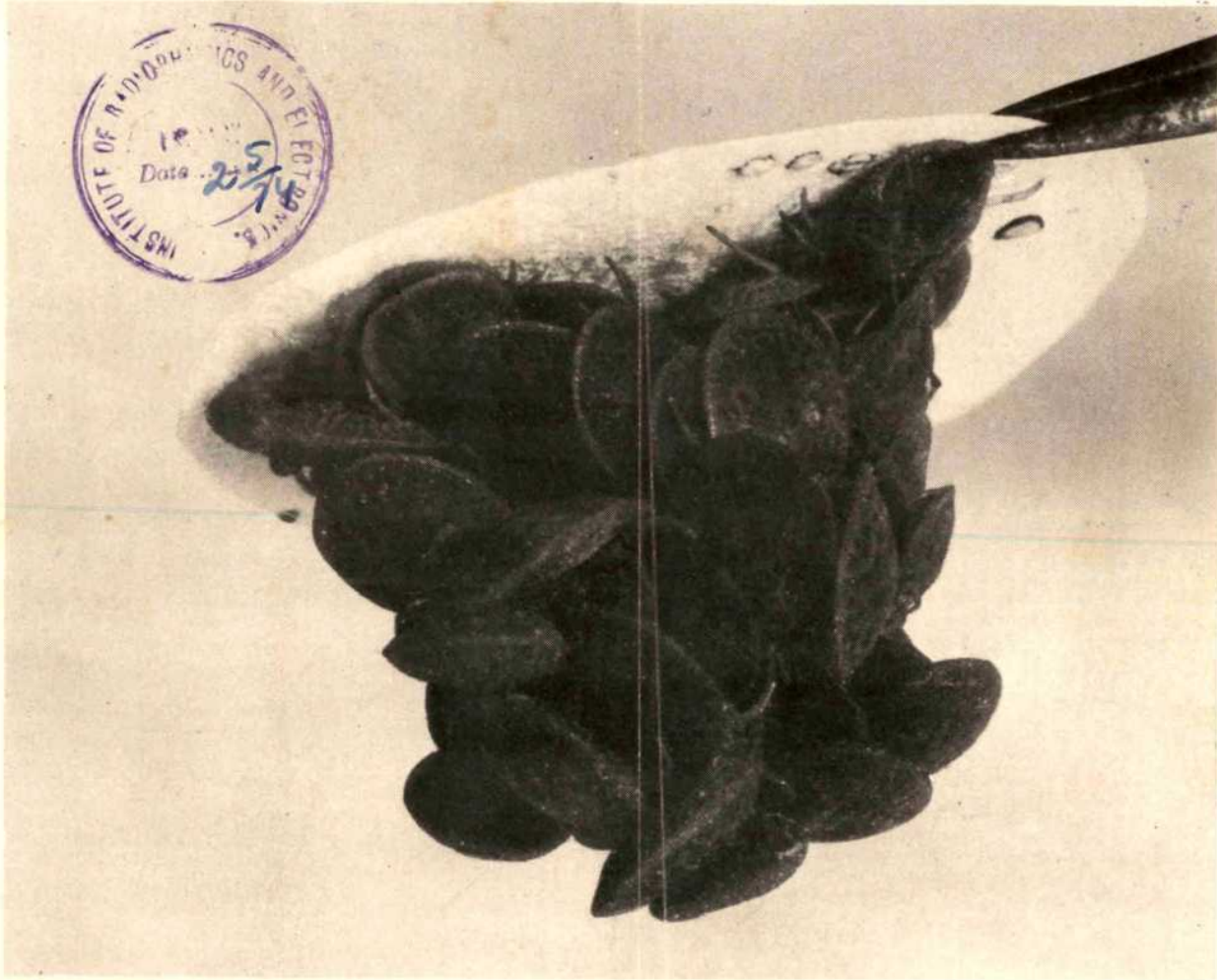
The final choice of candidates will be made by a National Selection Committee, comprising representatives of the universities and of ICI.

NATURE

Vol 246 No 5434

December 21/28 1973

FRIDAY



Tick assembly pheromones

Gastrin and arthritis
Human muscular dystrophy
Climatic change
Design of wind instruments

Cell

A journal of the molecular biology
of cells and their viruses

In January of 1974, The MIT Press will begin publication of **Cell**, a new monthly journal of cell and viral biology. Edited by Benjamin Lewin, formerly the editor of *Nature New Biology*, **Cell** will provide a wide-range journal publishing articles of general interest in molecular biology, cell biology, tumor virology and immunology, genetic development and other related areas. Papers will be refereed as rapidly as possible and those accepted will be published within twelve weeks.

Cell will also include an extensive review section. In addition to those reviews with the traditional role of discussing a field in some depth, short reviews will give conceptual accounts of recent advances in areas of cellular biology, for the benefit of researchers in other areas. Book reviews and discussions of meetings will also be included.

The January issue of **Cell** will include the following articles:

Genetically directed preferential X-activation seen in mice: U. Drews, S. R. Blecher, D. A. Owen and S. Ohno

Ouabain-resistant mutants of mouse and hamster cells in culture: R. M. Baker, D. M. Brunette, R. Mankovitz, L. H. Thompson, G. F. Whitmore, L. Siminovitch and J. E. Till

A uridine kinase-deficient mutant of 3T3 and a selective method for cells containing the enzyme: L. Medrano and H. Green

SpoT, a new genetic locus involved in the stringent response in *E. coli*: T. Laffler and J. Gallant •

The messenger-like poly-A containing RNA species from the mitochondria of mammals and insects: M. Hirsch, A. Spradling and S. Penman

Existence of methylated messenger RNA in mouse L cells: R. P. Perry and D. E. Kelley

Arrangement of specific oligonucleotides within poly-A terminated Hn RNA molecules: G. R. Molloy, W. R. Jelinek, M. Salditt and J. E. Darnell

Mixed splenocyte cultures and graft versus host reactions selectively induce an "S-tropic" murine type C virus: C. J. Sherr, M. M. Lieber and G. J. Todaro

Studies on the levels of cyclic AMP in cells transformed by wild type and temperature sensitive Kirsten sarcoma virus: R. A. Carchman, G. S. Johnson, I. Pastan and E. M. Scolnick

The February issue of **Cell** will include the following articles and reviews:

Viral Hepatitis, the B Antigen and Liver Cancer: A. J. Zuckerman

Integration and Excision of Phage Lambda: M. Gottesman

GUG and UUG are Initiation Codons In Vivo: J. H. Miller

The Molecular Biology of Tumour Viruses, edited by John Tooze: B. Mahy

Altered Metabolism of the Guanosine Tetraphosphate, ppGpp, in Mutants of *E. coli*: G. Stamminger and R. A. Lazzarini

Continuous Production of Radiation Leukemia Virus in C57BL Thymoma Tissue Culture Lines: Purification of the Leukemogenic Virus: M. Haas

Changes in RNA in Relation to Growth of the Fibroblast. I. Amounts of mRNA, rRNA and tRNA in Resting and Growing cells: L. Johnson, H. Abelson, H. Green and S. Penman

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OCEANOGRAPHY

Biological Oceanographic Processes

Timothy Parsons and Masayuki Takahashi,

Institute of Oceanography, University of British Columbia

196 pages 59 illustrations £4.00 hard cover £2.85 flexi cover

This book is an introductory text for students, physical oceanographers, engineers, hydrologists and fisheries experts who require some quantitative expressions of biological oceanographic phenomena. The first two chapters describe the composition and distribution of organisms in the plankton community as a prelude to later chapters. These deal with the primary formation of particulate material which is the beginning of the food chain in the pelagic food web; and the cyclic interdependence of all processes in the sea. The final chapter presents examples of problems in the marine environment which, the authors feel, require the particular attention of the biological oceanographer. These examples suggest where there is a basis for the solution of such problems, using some of the information contained in the rest of the book.

The Detection of Fish

David Cushing,

The Fisheries Laboratory, Lowestoft, Suffolk

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Progress in Oceanography

Edited by Bruce Warren,

Woods Hole Oceanographic Institute, Massachusetts

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	Page		Page
Living with No-growth	439	Physical Sciences	
World Health Organization and Genetic Disorders/Birth Defects	440	Seafloor spreading—TiO ₂ as a possible guide to past spreading rates—NISBET (Cambridge) and PEARCE (East Anglia)	468
NEWS		Geophysics—High resolution laser strainmeter—GOULTY, KING (Cambridge) and WALLARD (NPL, Teddington)	470
Nuclear Weapons in Europe/Research Spending/EPA/Coal/Short Notes	442	Seismology—Late aftershocks, tectonic stress and dilatancy—EVISON, ROBINSON (Wellington) and ARABASZ (DSIR, Wellington)	471
NEWS AND VIEWS		Glaciation—Interstadial site on the Island of Lewis—VON WEYMARN and EDWARDS (Aberdeen)	473
Wanted—A Taxonomist for Magnetism/Prospects for Hepatitis B Vaccines/Origin of Marginal Seas/Ribosomal RNA/Photosynthesis/Hormones/X-Ray Sources / Palaeomagnetism / Solar System / Zoology / Insecticides	445	Underground nuclear explosions—Multiple discriminant screening procedure for test ban verification—BASHAM and ANGLIN—(Department of Energy, Mines and Resources, Ottawa)	474
ARTICLES		Magnetism—New spin structure in an amorphous ferric gel—COEY and READMAN (CNRS, Grenoble)	476
Planetary Alignments, Solar Activity and Climatic Change—GRIBBIN (Nature)	453	Elastohydrodynamics—Optical elastohydrodynamics at extreme pressures—GENTLE (Royal Military College of Science, Shrivenham) and CAMERON (Imperial College, London)	478
Cyclic AMP—mRNA transcription linked to morphological and plasma membrane changes induced in tumour cells—KORINEK, SPELSBERG and MITCHELL (Vanderbilt School of Medicine)	455	Musical instruments—Speed of sound in bent tubes and its relevance to the design of wind instruments—BRINDLEY (Institute of Psychiatry, London)	479
Geophysics—Origin of the West Philippine Basin—KARIG (Cornell), INGLE (Stanford), BOUMA (Texas A & M), ELLIS (Marathon Oil Company, Littleton), HAILE (Malaya), KOIZUMI (College of General Education, Osaka), MACGREGOR (California, Davis), MOORE (California, Santa Cruz), UJIIE (National Science Museum, Tokyo), WATANABE (Tokyo), WHITE (Scripps Institution, La Jolla), YASUI (Meteorological College, Kashiwa) and YI LING (Washington)	458	Biological Sciences	
Elastin—Molecular model for elastin structure and function—GRAY, SANDBERG and FOSTER (Utah)	461	DNA polymerase—Inhibitor in sera of tumour-bearing mice—GOTTLIEB, SMITH, PLESCIA, PERSICO and NICHOLSON (Rutgers)	480
LETTERS TO NATURE		RNA—Use of ¹²⁵ I in fingerprinting RNA—DUBE (Max-Planck, Göttingen)	483
Physical Sciences		DNA repair—Endonuclease-sensitive sites in daughter DNA of ultraviolet-irradiated human cells—BUHL and REGAN (Tennessee)	484
Interstellar molecules—Radio detection of CH—RYDBECK, ELLDÉR and IRVINE (Onsala Space Observatory)	466	DNA sequences—Differences in murine leukaemia virus-specific DNA in normal and malignant cells—VIOLA (Harvard) and WHITE (NIH, Bethesda)	485
		Tumour cells—Biochemical parameters correlated with tumour cell implantation—BOSMANN, BIEBER, BROWN, CASE, GERSTEN, KIMMERER and LIONE (Rochester)	487

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C. H. Waddington *editor*. Radical exponents of the life-sciences holds a 'think-tank' on the Man-made future. Participants are Margaret Mead, John Papaioannou, C. G. Heden, John Platt, John Cage, Ruth Sager, Gunther Stent, and C. H. Waddington. 80 pp. 50p.

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F. R. Hodson and J. Doran

Mathematical Structure of Clinical Medicine

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Biological Sciences

Page

- Skin cancer**—Inhibition of carcinogen formation in skin irradiated with ultraviolet light—LO and BLACK (Houston) 489
- Carcinogenesis**—Dietary enhancement of intestinal carcinogenesis by dimethylhydrazine in rats—ROGERS and NEWBERNE (MIT, Cambridge) 491
- 'Asian cigarette'**—Adverse prognostic factor in peripheral disease—HILL, MOELIONO, TUMEWU, BRATAAMADJA and TOHARDI (Marantha University, Java) 492
- Cancer**— α -foetoprotein antibodies and foetal mortality in rabbits—SLADE (Wales, Aberystwyth) 493
- Serum progestins**—Luteinising hormone levels in non-suckled primiparous heifers—TRIBBLE, SORESEN, WOODWARD, CONNOR, BEVERLY and FLEEGER (Texas A & M) 494
- Immunological tolerance**—Is cortisol responsible for inhibition of MLC reactions by pregnancy plasma?—KASAKURA (Royal Victoria Hospital, Quebec) 496
- Inflammatory arthritis**—Animal model shows immunoreactive gastrin levels raised in inflammatory arthritis—ROONEY and DICK (Royal Infirmary, Glasgow), IMRIE (Beecham Research Laboratories, Betchworth) and BUCHANAN (Queen's, Belfast) 497
- Populations**—Existence of relationship between IQ and ABO blood groups—GIBSON (Cambridge), HARRISON, CLARKE and HIORNS (Oxford) 498
- Muscular dystrophy**—Collateral innervation of muscle fibres by motor axons of dystrophic motor units—DESMEDT and BORENSTEIN (Brussels) 500
- Caudal organ secretion**—Preliminary characterisation in adult and juvenile *Apodemus flavicollis* of both sexes—STODDART (King's College, London) 501
- Nerve growth factor**—Immunological properties of serum nerve growth factor—BANKS, BANTHORPE, CHARLWOOD, PEARCE, VERNON (University College London) and EDWARDS (Wellcome Research Laboratories, Beckenham) 503
- Vision**—Evidence for existence of neurones sensitive to direction of depth movement—REGAN and BEVERLEY (Keele) 504
- Visual cortex**—Experimental creation of unusual neuronal properties in kitten—VAN SLUYTERS and BLAKEMORE (Cambridge) 506
- Neurones**—Optical recording of impulses in individual neurones of an invertebrate central nervous system—SALZBERG, DAVILA and COHEN (Yale and Woods Hole) 508
- Electron microscopy**—Reconstruction of images from transforms by an optical method—GIBBS and ROWE (Leicester) 509
- Juvenile hormone**—Implicated in endocrine activity retained in diapause insect larvae—CHIPPENDALE and YIN (Missouri) 511
- Spermatozoa**—Dislocations in microtubular bundles within spermatozoa of the coccid insect *Neosteingelia texana* and evidence for slip—HARRIS (Witwatersrand) and ROBISON (Virginia and NIH, Bethesda) 513
- Pheromones**—Assembly pheromone(s) in a soft tick—LEAHY (Mount St Mary's College, Los Angeles), VANDEHEY (St Norbert College, Wisconsin) and GALUN (Israel Institute for Biological Research, Ness Ziona) 515
- Vision**—Properties of visual pigment of the freshwater stingray—MUNTZ, CHURCH and DARTNALL (Sussex) 517
- Population genetics**—Polymorphic marker to detect origin of the European eel—DE LIGNY (Nether-

Biological Sciences

Page

- PCB residues**—Presence in plankton from the Gulf of St Lawrence—WARE and ADDISON (Bedford Institute of Oceanography, Dartmouth, Nova Scotia) 519
- Immunology**—Antibody response to tapeworm *Hymenolepis diminuta* in the rat—HARRIS (Wellcome Research Laboratories, Beckenham) and TURTON (Oxford Polytechnic) 521
- Decompression**—Ultrasonic surveillance of subatmospheric decompression—EVANS, WALDER (MRC, Royal Victoria Infirmary, Newcastle upon Tyne) and MACMILLAN (RAF Institute of Aviation Medicine, Farnborough) 522
- Cardiotoxic protein**—Isolation of a new cardiotoxic protein from the edible mushroom, *Volvariella volvacea*—LIN, JENG, CHEN, SHI and TUNG (Taiwan) 524
- Bacterial motility**—Loss under pressure—MEGANATHAN and MARQUIS (Rochester) 525
- Bacterial metabolism**—Formation of calcite crystals is a general phenomenon—BOQUET, BORONAT and ROMOS-CORMENZANA (Barcelona) 527
- Mitosis**—Origin of chromosome number variation in cultured plant cells—BAYLISS (Leicester) 529
- Protein evolution**—Periodicity in high-sulphur proteins from wool—ELLEMAN, LINDLEY and ROWLANDS (CSIRO, Victoria) 530
- Indian Hipparion**—Reply to assertion of first appearance in Nagri and not Chingi deposits—HUS-SAIN (Howard University, Washington) 531

GENERAL

- Psychology**—What children do in spite of adults' hypotheses—BOYSSON-BARDIES and O'REGAN (CNRS, Paris) 531

BOOK REVIEWS

- The Evolution of Melanism: The Study of a Recurring Necessity, with Special Reference to Industrial Melanism in the Lepidoptera, Bernard Kettlewell (P. M. SHEPPARD) 535
- The Estimation of Animal Abundance and Related Parameters, G. A. F. Seber (R. K. MURTON) 536
- Causal Thinking in the Health Sciences: Concepts and Strategies of Epidemiology, Mervyn Susser (P. D. OLDHAM) 536
- Past and Present Vegetation of the Isle of Skye: a Palaeoecological Study, H. J. B. Birks (PETER D. MOORE) 537
- Experimental Embryology of Echinoderms, Sven Hörstadius (D. R. NEWTH) 537
- Theoretical Physics: an Advanced Text. Volume 3: Quantum Mechanics, Benjamin G. Levich, V. A. Myamlin and Yu A. Ydovin (E. LEADER) 537
- The Shape and Structure of Molecules, C. A. Coulson (T. H. K. BARRON) 538
- Stable Isotope Geochemistry, John Hoefs (J. R. MAXWELL) 538

CORRESPONDENCE

- Television (Robert Reid)/DNA Methylation (Eduardo Scarano)/Soviet Science (J. W. Jeffery)/Smoking and Pregnancy (Bea J. van den Berg)/Smoking, Pregnancy and Publicity (Harvey Goldstein)/Literature Citations (Michael Yarmolinsky and Marie-Joelle Hoogveld-Lepasteur)/Bomb disposal (George Davidson)/Foraminifera M. D. Brasier; John R. Haynes 539

OBITUARY

Synopsis of the British Fauna (New Series) No. 4

British Harvestmen**Arachnida: Opiliones****Keys and Notes for the Identification of the Species****J. H. P. Sankey and T. H. Savory****January 1974, approx. 80 pp., approx. £1.60/\$4.50**

0.12.619050.X

This volume is more than a mere systematic description of all the British species of harvestmen: it includes accounts of their behaviour and physiology as well as aspects of their biology and distribution. A key for the identification of the species is given and some reference to their individual histories. The book is illustrated with simple, clean figures and forms the most recent work in this field of arachnology and should prove a welcome laboratory and field guide for amateur and professional naturalists.

Physical Chemistry of Melts in Metallurgy Volume I**F. D. Richardson FRS****January 1974, approx. 320 pp., approx. £6.50/\$18.25**

0.12.587901.6

Outlining our present knowledge concerning the chemistry of liquid melts, salts, mattes and slags, this two volume publication forms a selective work aimed at highlighting those systems which exemplify important principles or which are of industrial importance. This is the first work which brings together our knowledge of structural kinetic and thermodynamic properties of melts important in metallurgy, and considers the kinetics of reactions between them in terms of chemical, electrochemical and mass transfer phenomena.

Contents:**Structure and Kinetic Properties:** Liquid metals. Ionic melts. Polymeric melts.**Thermodynamic Properties I:** Thermodynamics of solutions. Metal solutions. Salt melts. Polymeric melts.**Biology of Plant Litter Decomposition Volume I****Edited by C. H. Dickinson and G. J. F. Pugh****January 1974, xlv+288 pp., £7.00/\$19.75**

0.12.215001.5

This two volume publication is unusual in that it treats ecological problems in a truly biological manner, analysing separately the influences of litter type, organisms, and the environment, on litter decomposition, as well as identifying those areas which demand future investigation. A comprehensive approach to the subject has been adopted by the editors, who aim to correlate knowledge on litter decomposition, by relating it, for instance, to the marine environment, or to single groups of animals.

Contents of Volume I

J. E. Satchell: Introduction. **Types of Litter:** **J. C. Frankland:** Decomposition of lower plants. **M. K. Bell:** Decomposition of herbaceous litter. **V. Jensen:** Decomposition of angiosperm tree leaf litter. **C. S. Millar:** Decomposition of coniferous leaf litter. **A. A. Käärik:** Decomposition of wood. **J. S. Waid:** Decomposition of roots. **B. C. Lodha:** Decomposition of digested litter. **Organism Index. Author Index. Subject Index.**

Displacement of Water and its Control of Biochemical Reactions**Sherry Lewin****January 1974, approx. 400 pp., approx. £7.00/\$19.75**

0.12.446250.2

Although all biochemical activities take place in aqueous media, little attention has been paid to the dynamic control which water displacement can exercise in biochemical reactions. Using simple, concise language and a minimal amount of mathematics, this book presents a novel and unified approach which combines stereo-chemical with energy considerations and illustrates the influence that H... bonded interactions of hydrophilic groups and of adherence of hydrophobic groups can exercise on biochemical reactions, by virtue of the entropy change of accompanying water displacements.

This book is directed to biologists—whether biochemists, molecular biologists, immunologists, physiologists, bacteriologists or virologists. Indeed, all scientists whose interests embrace water activities, biological helices, H... bond direction, and evolution should find this book thought-provoking and useful.

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Living with No-growth

THERE has been a remarkable transition in the past few weeks from a situation in which energy was a nagging middle term concern, to be dealt with by orderly readjustment of priorities, to that which prevails now, in which fuel shortages are commonplace and even desperate measures may be ineffectual. The consequences of this sudden crisis can barely be guessed yet, because although it is indisputable that oil prices in the future will be much higher, it is an open question whether oil will ever flow as freely again. The view from Britain is bound to be coloured by the simultaneous progressive seizing up of the electricity and coal industries and the railways on account of industrial action. Nevertheless the situation can hardly be said to be other than gloomy in any industrialised society.

The cutback in oil supplies has some advantages to it. At a stroke, it highlights the extraordinary way in which we have been acquiring energy cheaply and squandering it. Certainly no government would have been able to impose restrictions on home heating, office lighting, high speed driving, flying half-empty aircraft and sundry other current affectations in the absence of such a visible crisis. Yet now there is little complaint at such impositions and no doubt that such moderation in our habits will become part of our way of life.

Further lessons in restraint should also be sinking in. Military ventures by countries less than self-sufficient in oil and capable of supplying the huge increase in demand that war generates will be out of the question. This may not hold back the Soviet Union, but the United States, which has allowed itself to be lured by the deception of cheap energy into becoming an importer of fuel despite its huge resources, must temper its military policies unless it wants the North-east to freeze to death.

It is necessary to think beyond the immediate problems, however, and there is little doubt that the impact on science of the discontinuous change in the economic situation will be very serious. Economic growth for 1974 has been abandoned, implicitly if not explicitly, in many countries. A reduction in oil supplies, even temporary, makes even a stationary gross national product a difficult target to reach.

For a long time economists have debated the pros and cons of a no-growth economy and the arguments in favour of such a concept have become more appealing, if not yet compelling, in recent years. The Fall 1973 issue of *Daedalus* is devoted to a scholarly debate on the subject, which makes for interesting reading now that no-growth is thrust upon us, rather than, as even its keenest advocates would have, being introduced over a space of years.

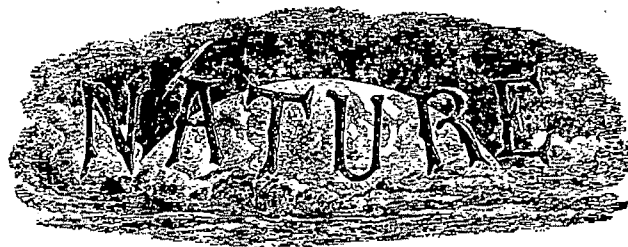
Growth, as Harvey Brooks puts it, "provides opportunities for talented or ambitious people to rise in social status and income without depriving others of status". If there is no growth then nobody can prosper without another faltering and there is palpably a great social need to ensure that if there is to be any income redistribution it is such that those at the bottom gain at the expense

of those at the top. But what is true for individuals is also true for institutions. Any spell of no-growth will at best freeze government spending and may well reduce it substantially, as such spending is an easily manipulated economic tool. It is very difficult to see how science budgets strongly dependent on government funds could remain intact under these circumstances. No-growth could never produce an Apollo programme, indeed Mancur Olson goes even further, "there would be few if any frontiers . . . in a no-growth society".

The problem is not purely a British one, although Britain in its present predicament would feel the effects of an unplanned stoppage of growth most keenly and most quickly. All industrial societies with growth targets that now have to be lowered will experience severe conflicts over priorities, and science is likely to come out the loser, especially when in competition with schools and hospitals for the same money. Such a situation could presumably render a large number of scientists redundant. A preferable alternative is that governments will see that even if they cannot hold the line on pure science they can justifiably switch scientific manpower to social needs programmes.

If the situation is not good in industrial countries, it is little short of appalling in the developing world. Even for those countries that the producers exempt from oil cuts, the rise in the price of oil must do damage to economies at a time when the prospects for improved aid from richer countries are negligible. It is not out of place to question whether science and scientific institutions can survive at all in developing countries.

100 Years Ago



- THE Council of the Society of Arts have given notice of their intention to provide a short course of lectures suitable for a juvenile auditory during the Christmas holidays. For this purpose arrangements have been made with Mr. Frank Buckland, M.A., Her Majesty's Inspector of Salmon Fisheries, to deliver two lectures "On the Structure and Habits of Beasts, Birds, and Fishes, as showing Beauty and Design," on Friday, January 2, and Friday, January 9, at 8 P.M. The lectures will be illustrated by specimens. It is intended to make every effort to obtain an entirely juvenile audience, and the notice in the Society's *Journal* impresses strongly upon the members the fact that only children, not adults, are wanted.

From *Nature*, 9, 151, December 25, 1873.

World Health Organization and Genetic Disorders

In *Nature* of June 22 (243, 433; 1973) Professor J. H. Edwards of the Department of Human Genetics at the University of Birmingham commented on the World Health Organization Report Number 497 on *Genetic Disorders: Prevention, Treatment and Rehabilitation*. In this article the group which prepared the report responds to the criticisms of Professor Edwards, who replies.

PROFESSOR J. H. EDWARDS'S quixotic commentary on the WHO report on the prevention, treatment and rehabilitation of genetic disorders should be corrected for the record.

He objects to the first paragraph of the report which refers to the "relative increase in morbidity and mortality attributable to [genetic factors resulting from] slow changes in gene frequencies". The phrase was quoted incorrectly (the portion in brackets was omitted) and out of context by Professor Edwards; it is one of three phrases which briefly introduce the concept that genetic disease is now of greater importance compared with its relative insignificance in the preceding decades of medical practice. Moreover, it would seem implicit that, if genetic disorders are diagnosed and treated in such a way as to alter fitness to any degree, gene frequencies will gradually reach a new equilibrium in man.

Reliability

Professor Edwards does not accept the statement that there is "no reliable information on the current prevalence of genetic disease", a phrase his reader thus sees in isolation because he again quotes out of context. The pertinent paragraph in the WHO report adumbrates: "or on the effects that treatment and prevention will have on the number of cases; there are problems that now need to be studied. Frequencies of individual traits will vary with geographic region, ethnic group, isolate, and deme. The surveys must be both general and particular, and their findings will have both broad and specific objectives. Accurate knowledge about the epidemiology of genetic disease is an important prerequisite of action by a particular community concerning prevention, treatment, and rehabilitation". It was the concern of our group that general information on prevalence of genetic disease, some of which is cited in Tables 2, 3 and 4 of Annex 1 to the report, should not be extrapolated uncritically to specific communities where

such data may not be currently available. Professor Edwards then declares "in fact, the (current) information is adequate for practical purposes; the numbers of the deaf, the blind, and the ineducable are known in all countries with compulsory education, and the proportions of these due to Mendelian and chromosomal disorders have been estimated on good data". Surely Professor Edwards does not believe that the deaf, blind and ineducable represent the only genetic diseases that need to be considered 'for practical purposes', and that compulsory education is the only bench mark of concern for his fellow man.

Meaning

Professor Edwards says that "the word genic is extended from its regular use to include multifactorially determined disorders". Multifactorial disorders are indeed genic, at least in the component which is genetically determined, he would surely agree! The concept of multifactorial disease as we described it was carefully defined but he has chosen not to quote those portions of the report. In the same paragraph, he refers to "a table on multifactorial disorders" in which "congenital malformations and conditions of unknown and non-genetic disease are used as exclusive categories". There is no such table in the report. If he had been accurate and referred his readers to Table 1 of Annex 1, which described the frequency of genetic disorders among patients admitted to a paediatric hospital, they would find that the categories therein are not intended to be exclusive. On the preceding page, it was explained that the classification "unknown" refers to: hospital admissions, not classifiable according to the McKusick catalogue of Mendelian inheritance in man (autosomal recessive, autosomal dominant, and X-linked disease), or the current classifications of chromosomal disease, or the NIH catalogue of congenital malformations; one third of which may possibly be hereditary conditions. On

this basis, we must disagree with Professor Edwards that "multifactorial" means the same thing as "of unknown aetiology". We are aware of Professor Edwards's views on the subject; unfortunately he did not tell his readers the difference between his views and our specific use of simple and carefully defined terms.

On page 31 of the WHO report, a mutation rate of 10^{-4} is used to demonstrate a very slow doubling time for the frequency of a rare recessive gene even with such an enormous mutation rate. It is quite clear the report did not intend the reader to assume that mutation rates in man are uniformly of this magnitude. Professor Edwards's carping at this point, taken out of context, is again misleading and unfair to his readers.

It is false for Professor Edwards to say: "genetic counselling urging couples (heterozygous for deleterious recessive genes) to total abstinence from reproduction is recommended". On page 33 of the report, it merely says that this procedure would be a slightly more effective method for high-risk patients to reduce the frequency of genetic disease than prenatal diagnosis with selective termination of pregnancy. Furthermore, the report states (page 34) "in the case of rare recessive genes, artificial selection against heterozygotes would be folly since every zygote is estimated to carry one or two deleterious genes". It is surprising that Professor Edwards then associates the former comment with the fact that almost everybody is a carrier of recessive deleterious alleles. Perhaps he failed to read the report carefully enough to assimilate the latter commentary. Fortunately we are usually carriers of alleles which are different from those of our spouses; only when two spouses are carriers of the same deleterious allele would genetic counselling be relevant, as Professor Edwards very well knows.

Claims

Professor Edwards takes exception to the "remarkable claim that cystic fibrosis (and sickle cell disease) can be diagnosed *in utero*". He is referring to material appearing in a table listed as Annex 2. Again, he cites the above-mentioned items out of context and without reference to the relevant material in the main body of the text (pages 19 to 21) where the appropriate cautions about prenatal diagnosis are stated. Only those hereditary diseases

eligible for prenatal diagnosis at the time the Scientific Group met (November 1971) are listed in the Annex; those which had actually been diagnosed *in utero* are printed in italics. Neither sickle cell disease nor cystic fibrosis is printed in italics; moreover, the former is keyed to a footnote which indicates that, since the condition is known to be genetically heterogeneous, particular care must be taken with those methods which at the time were thought to be of some use in prenatal diagnosis of this particular disease. The literature sources of the material in the table are clearly stated on the same page of the WHO report. Professor Edwards or any careful reader can obtain the details by reading the source material—as we did.

Professor Edwards criticises our use of compound interest to estimate the doubling time for multifactorial disorders, as cited in the final pages of the report (Annex 3). Although he criticises this approach, he does not suggest an alternative. The final graph, showing the time in generations required to double the frequency of harmful genes for single gene diseases, should reassure Professor Edwards rather than alarm him; doubling times of 1,000 or 100 or even 10 generations would hardly seem alarming, especially for frequencies so minute.

While we are waiting for Professor Edwards's precious grail of "orderly development of either practice or theory" to be found, we hope that he will permit those who have access to the report to use the great part of its 46 pages which escaped unscathed from his comments, for the purposes intended, namely, to begin to apply current genetic knowledge to the immediate benefit of the patient with genetic disease.

Error

We, "an assembly of experts with a dedicated secretariat . . . appropriately stratified by hemisphere, power block and language", remain grateful to Professor Edwards for pointing out an error in the report. We stated that relaxed selection, acting over 100 generations, would increase the frequency of a trait from 0.001 to 0.0086; the correct final frequency should be 0.0102. We fail, however, to see how this or any other alleged error in the report affected the conclusions that were drawn by the committee. If, as Professor Edwards asserts, "some" of the "doubtful assumptions, erroneous facts and uncertain inferences" he finds in the report "overflow into recommendations", would it be too much to ask how correction of a single one of the "errors" he cites would, or should, have altered the recommendations the committee made?

CHARLES R. SCRIVER CHAIRMAN

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PROFESSOR EDWARDS writes: Quotations are by nature out of context, and any obtuseness in understanding that small fraction of this technical report which was not technical, and which, rightly or wrongly, I considered could lead to an exaggerated claim of the need for counselling, must be left to the reader. So far as Annex 1 goes it seems reasonable to regard categories specified by percentages which sum to 100% as exclusive. In Annex 2 the heading "All the diseases in the following list can now be diagnosed prenatally" also seems clear. I was certainly in error in overlooking the conditional following the unfortunate apposition of "counsel" and "urge".

I do not think I am alone in feeling some anxiety at the casualness with which genetic counselling is being advanced as a salve for the problems of either our natural variability or for the therapeutic intractability of some of its consequences and, where emotion and enthusiasm run high, there is no substitute for precision in word and number and caution in application. The greater the expertness of a committee, or the weight of authority of the organisation, or its area of influence, or the distinction of its previous reports, the greater the need to expose to public accountancy any doubtful claims which may be influential. I am not doubting the benefits available to the populations of, for example, Montreal or Moscow, or the advantages of their wider availability, provided that they are subordinated to an efficient administration for diagnosis and therapy and do not compete with this basic requirement in the allocation of funds. I am doubting the scale of benefits to populations of counselling *per se* and disturbed at the casual widening in terminology by which counselling is extended to diagnosis and unsolicited advice, therapy to selective abortion, genetic disease to multifactorial disease (I hardly claim any originality for the view that all diseases are multifactorial, but some are less multifactorial than others), and prevention to elimination. In neither Montreal nor Moscow, nor in any other city, would I wish to see unsolicited genetic counselling being given on the basis of computerised files of so-called multifactorial disease (which includes schizophrenia) in relatives. I do not share the optimism of the group which "is convinced that genetic registries can be designed and used in ways that will contribute to the diagnosis and prevention of genetic disease without

endangering individual rights", unless genetic is used in the restricted sense which excludes multifactorial, or the registries are decentralised and maintained within hospital records departments. Quixotry implies an aggressive and well-intended reaction to a delusion and, while I hope my anxieties are delusions, I remain unconvinced.

It would be a great tragedy if drawing attention to any apparent *non sequiturs* should in any way be regarded as critical of the technical reports in general, or of the administration under which they are edited. Effective documents are necessarily controversial and the genetic future of man is too important a subject to be constrained by the niceties of private dissent.

BIRTH DEFECTS

Hope for Spina Bifida

SINCE the publication of the WHO report number 497 there have been several advances in the prediction in the uterus of a defective embryo. Perhaps the most significant of these has been the discovery that fetuses which are anencephalic or which suffer from spina bifida release a high amount of alpha foetoprotein into the amniotic fluid. This high protein level, if detected as a result of amniocentesis, is a sign of a deformed foetus.

In Britain about 2,000 anencephalic children, and a similar number of spina bifida cases are born annually. In principle these births can now be avoided if a positive amniocentesis is followed by abortion.

It is, however, impracticable to study every pregnancy in Britain (731,000 births in 1972). Therefore the discovery by Dr D. J. H. Brock and colleagues at the University of Edinburgh (*Lancet*, ii, 923; 1973) that for anencephaly an excess of alpha foetoprotein is found in maternal blood, is welcome.

Spina bifida, however, throws up greater problems than anencephaly for such children who undergo surgery soon after birth, live for a long time, although they are usually both physically and mentally handicapped afterwards. Anencephalic children die at birth.

An excess of alpha foetoprotein is also found in the blood of some mothers who are carrying spina bifida fetuses but Dr Brock said this week that the test on maternal blood was not as reliable as in the case of anencephaly. It seems that an excess of protein is found when the foetus is very deformed but when the deformation is slight there is not always a detectable amount of the protein in the blood.

NEWS

Nuclear Weapons in Europe

by our Washington Correspondent

A RARE glimpse of the extent and nature of the nuclear umbrella that the United States has erected over Europe is provided in a report prepared by staff members of the Senate Foreign Relations Committee. It indicates, among other things, that as many as 7,000 nuclear warheads are stockpiled in more than 100 special ammunition sites throughout Europe and, although all the weapons are in United States custody, about two-thirds of them are for use by European forces. Some of the weapons are constantly loaded, ready to be unleashed on command.

The report has been heavily censored by the Department of Defense and it is tantalisingly devoid of detail. Nevertheless, it lifts a fraction of the veil of secrecy that surrounds European nuclear defence planning and it brings together—and confers official status on—information which has previously appeared unofficially in the public record. It also emphasises the extent to which Europe is dependent on the United States for its defence.

Although delivery systems capable of carrying nuclear weapons were deployed by the United States in Europe during the 1950s, warheads were not stockpiled until President Eisenhower formally proposed the idea at a NATO Heads of Government meeting in 1957. Since then, the buildup of American nuclear weapons in European bases has been governed by a set of bilateral agreements between the United States and individual European governments. One of the agreements provides that the location of storage sites is to be determined by the NATO Supreme Allied Commander in Europe (SACEUR)—who is also commander in chief of American forces in Europe—in agreement with United States military authorities and the government of the country concerned. The agreements also specify that the weapons will remain in the custody of United States personnel, and that the 'user country' will pay the costs of stockpiling them.

The bilateral agreements are broad and they do not identify individual nuclear weapons systems. In fact, the Senate committee report states that it was not until 1967—a full ten years after stockpiling began—that the United States finally agreed to provide Euro-

pean governments with details of the nuclear weapons stockpiled in their territory or stored elsewhere for use of their troops. (That revelation begs the question of how NATO managed to carry out sensible defence planning without knowing the nature of the weapons that the United States had installed in Europe.)

Robert S. McNamara, Secretary of Defense, announced in 1966 that there were then some 7,000 nuclear warheads stockpiled in Europe, a figure which the report notes "was the first, last and only official revelation regarding the size and disposition of the American nuclear armory in Europe". The total has since fluctuated and the present level has been deleted from the report, but 80% of the land-based warheads are for tactical weapons which can be used for offence or defence and the rest are purely defensive.

The warheads are stored in special

igloos, in sites surrounded by double fences which are floodlit at night. Some of the weapons, including a proportion of those for use by European forces, are always maintained on what is termed quick reaction alert, ready to be fired as soon as the order is given. The proportion of the total nuclear force which is ready to be unleashed depends on the general state of alert in the NATO forces.

An agreement drawn up by NATO members in 1969 provides for consultation among member governments before nuclear weapons are used in Europe. According to the Senate report, it would work like this. A request for the use of nuclear weapons in the defence of NATO, which comes from either a member government or from a major NATO commander, or any possibility that a nuclear power may use nuclear weapons to defend NATO, will be communicated immediately to all NATO

RESEARCH SPENDING

Battelle Forecast of Increase

by our Washington Correspondent

ESTIMATING the amount of money that will be spent on research and development in 1974 is a risky business, particularly in the light of the great uncertainties in the economic outlook. Nevertheless, according to the annual forecast of the Battelle-Columbus Laboratories, the total amount to be spent on research and development in the United States next year is expected to reach about \$32,400 million—an increase of some \$2,300 million over this year's expenditure. The Battelle forecast is perhaps the most widely expected of all the exercises in crystal-ball gazing that are carried out in the United States to predict funding for research and development.

Although the expected increase would be mostly swallowed up by inflation—which is reckoned to be running at about 5% for research and development costs—it would nevertheless, represent a modest growth in purchasing power. Industry is expected to provide a relatively large increase in research funds and support from the Federal Government is also expected to grow, according to the report.

Battelle acknowledges, however, that the forecast could be upset by energy shortages and other factors. On the one hand, if the energy crisis leads to widespread recession, industrial research and development could be hard hit. But, on the other, the energy crisis is likely to stimulate increased research and development on energy production and conservation.

The forecast sees the Federal Government providing about \$16,800 million, industry more than \$13,700 million, universities and colleges about \$1,500 million and non-profit institutions about \$480 million. Industry is therefore expected to provide about 42% of the total research and development funding next year, compared with 31% ten years ago. But the increases will not come from every industrial sector, for the forecast predicts that four industrial groups—food manufacturers, chemical companies, instrument makers and producers of electrical machinery—will increase their research and development funding at a rate greater than the rate of inflation. Expenditures by other industry groups will probably not even keep pace with inflation.

governments and to the Defense Planning Committee (a top level committee consisting of all NATO members except France). The views of the individual governments and of the Defense Planning Committee would then be transmitted to the nuclear power concerned. In other words, the Supreme Allied Commander in Europe would "not be permitted to use nuclear weapons unless there were consultations with NATO member governments directly and with NATO itself".

In the final analysis, however, only the President of the United States or, for British nuclear weapons, the British Prime Minister, can authorise the release of nuclear weapons. Thus Presidential approval would be required before any use of United States nuclear weapons by NATO forces.

The Senate report outlines general NATO strategy with respect to both conventional and nuclear forces, the basic elements of which are "nuclear deterrence, forward defense and flexible response". Should deterrence fail, there are three levels of military response open to allied forces. "The first is direct defense—that is, defeating the enemy on the level he chooses to fight, a concept which includes the use of such available nuclear weapons as may be authorised". The second level of response would be "deliberately raising, but where possible controlling, the scope and intensity of combat, making cost and risk disproportionate to the aggressor's objectives and the threat of nuclear response progressively more imminent". The final response would be "massive nuclear strikes against the total nuclear threat, other military targets and urban industrial targets". The ultimate general nuclear response could, however, be carried out only in conjunction with the United States Joint Chiefs of Staff plan for widespread synchronised use of United States nuclear weapons. "Accordingly", the report notes, "responsibility for carrying out NATO's general nuclear response falls on US strategic forces based outside Europe".

EPA

Appearing Objective

by our Washington Correspondent

MR RUSSELL TRAIN, the new Administrator of the United States Environmental Protection Agency (EPA), has decided to cut off a subsidy that the agency provides to an industrial research organisation because of public allegations that the subsidy compromises the EPA's regulation of automobile pollution. The organisation concerned is the Coordinating Research Council-Air Pollution Research Advisory Committee

(CRC-APRAC), a research organisation supported by the automobile industry, the oil industry and the EPA. It has sponsored some of the key research on which many emission control regulations have been based.

The decision to sever ties between the EPA and CRC-APRAC was based on a review conducted by Mr Train shortly after he became administrator of the agency. He explained in a letter to Mr M. K. McLeod, director of CRC-APRAC, that although he is entirely satisfied that the organisation's work has been objective and free from bias, "not only the fact of objectivity but also the appearance of objectivity must be considered when it comes to evaluating continued EPA participation in this activity".

CRC-APRAC receives three-quarters of its money from the American Petroleum Institute and the Motor Vehicles Manufacturing Association, both of which are industrial organisations, and the rest from the EPA. It funds research on the effects on health of automobile emissions, on emission control technology and on vehicle testing.

The chief criticisms of the agency's ties with CRC-APRAC have come from Senator Edmund S. Muskie, Chairman of the Subcommittee on Air and Water Pollution, and the chief sponsor of pollution control measures in the Senate. He has charged that the organisation's advisory committee, on which representatives of the automobile and oil industries predominate, decides, without outside advice, what research should be undertaken; that the research is then monitored by panels which are also dominated by industry representatives; and that the results eventually wind up as the basis for regulations vitally affecting the industries concerned.

As evidence of conflict of interest in CRC-APRAC, Muskie published an internal EPA memorandum in the *Congressional Record* last week which discusses the motor industry's attitudes to the EPA's programme to control emissions from heavy-duty diesel engines. According to the memorandum, an official of Cummins Engine, one of the two largest manufacturers of diesel engines in the United States, said in a discussion that the CRC-APRAC programme to develop new test procedures for heavy-duty engines/vehicles was the most "effective coup that the industry has pulled off on EPA" as it commits the EPA to a long and complicated project which could postpone instituting controls for heavy-duty engines for many years.

In addition to severing its formal ties with CRC-APRAC, the EPA has decided to take over the management and funding of three projects which are now being carried out under the organisation's auspices.

COAL

Aggregated Waste

DAMAGING though the miners' overtime ban may be to the National Coal Board (NCB) there is one section of the board that has its problems temporarily eased. The Minestone Executive is responsible for the 50 million tons of spoil that emerge from the ground each year along with the coal. While the overtime ban is on, the quantities are at least a little smaller.

With the increasing mechanisation of the coal industry the quantities of waste produced have risen sharply. Machine mining often takes parts of the roof and floor away at the same time as the coal and this extra waste travels up to the surface.

But attempts to do anything with the shale that was accumulating in massive tips in the mining areas are relatively recent. Only in the past fifteen years has a serious effort been made. It is estimated currently that the coal board has in the region of 3,000 million tons of spoil lying around Britain.

Now that local authorities have tightened up on their planning procedures new tips are hard to start and old tips are frowned on, so the NCB has the job of tidying up the past and preventing desecration in the future.

Finding uses for the shale has never been easy. Several million tons have been used as fill for motorways. About half a million tons a year have been turned into bricks by the Scottish and the Midland Brick Companies, and some spoil has been turned into a base matrix for the extremely tough but very expensive Guyana bauxites. This mix has a high skid resistance and has been put on Britain's crossroads particularly in the Greater London Council area. But, beneficial though this use is, the tonnage involved are relatively small.

With the large motorway programme in the coalfield areas coming to an end the demand for spoil as a motorway fill is decreasing. Although major road works will still need the spoil, the sharper bends and steeper hills allowed on main roads will cut the demand.

But with the oil shortage certain to increase the cost of transport, colliery spoil could benefit. Transport is the highest part of the cost of any shale. With the coal fields in the centre and in the north of Britain it could become economically attractive to use closer, although less satisfactory, shales from collieries than to go further afield for a higher quality stone.

The best future use for shale may lie in the aggregates business. The Verney Committee, set up by the Department of the Environment, produced a preliminary report recently in which it stated that current demand for aggregates is around 220 million tonnes a

year; a figure that will rise to 330 million tonnes a year by 1980.

The committee urged that more research should go into alternative aggregate supplies—which includes the NCB's spoil. The availability of sand and gravel from pits and quarries is becoming more limited—particularly in the south-east—and environmental considerations are coming into play.

As a first step to large scale commercial aggregate production, a half million ton a day plant is being built at Snowdown in Kent.

This aggregate is lightweight material which will probably be used for cladding purposes rather than as structural concrete. The British lightweight aggregate market runs at about 4 million tons per annum at present, but with natural aggregate becoming scarcer and more expensive there may well be a larger market available to the board in the manufactured aggregate field.

If it were decided to get rid of the spoil heaps by any available method, the board has calculated that there is five times as much space available in quarries as there is spoil on the surface.

Short Notes

Another Leap Second

EVIDENCE that the Earth continues to run slow comes from the Time Department of the Royal Greenwich Observatory, which has announced that the atomic time signals will be retarded by 1 second at midnight on December 31. This is done by inserting a so-called time step, or leap second, into the time signals so that the familiar BBC six-pip signal becomes seven pips.

This is the third time step that has had to be added since the atomic standard was introduced at the start of 1972. By agreement, the atomic time signals are not normally allowed to diverge from universal time (UT or GMT) by more than 0.7 s.

Currently, the Earth loses about 3 ms a day on Atomic Time, and the leap seconds are added where necessary—preferably at the end of June and/or December—to keep UT and Atomic Time in close correspondence.

By the end of December the Atomic Time signal will be 0.3 s ahead of UT. After the time step, Atomic Time will lag UT by 0.7 s. When the next time step has to be introduced will depend on how UT flips back with respect to Atomic Time during 1974.

Prostaglandin on the US Market

THIRTEEN months after its introduction in the United Kingdom, a prostaglandin has become commercially available on a similar basis in the United States. The United States Food and Drug Admini-

stration has permitted limited distribution to hospitals and clinics of Prostin $F_{2\alpha}$, known in the laboratory as prostaglandin $F_{2\alpha}$, one of the family of compounds considered to hold promise for treatment of such conditions as asthma, ulcers and high blood pressure, as well as for their ability to induce uterine contractions. The drug, developed and produced by the Upjohn Co., Kalamazoo, Michigan, will be used specifically for the induction of abortion during the second trimester of pregnancy—the fourth to sixth month. At this stage Prostin $F_{2\alpha}$ will be sold only to university medical centres where it has already been used in research or where physicians are familiar with the techniques involved in its administration. These presumably comprise chiefly the obstetricians who gathered at Upjohn's conference centre, Brook Lodge, in Michigan, in June 1972 to discuss the progress of their clinical trials (*Nature*, **237**, 482; 1972). At that time the most satisfactory mode of administration during the second trimester seemed to be direct injection into the amniotic sac and Prostin $F_{2\alpha}$ has been produced in a form suitable for use in this way.

Artistic Talent

THE Medical Art Society is extending an invitation to scientists who sculpt or paint to exhibit with the society at its exhibition in London in 1974.

Scientists are particularly invited to contribute to the section of the exhibition called "intraism". The society describes what this means as follows. "Portrayal of the 'hidden' and portrayal of the 'minutiae' are the goals we of this century can achieve in the three modalities of representation termable intra-realism, intra-impressionism and intra-abstraction".

As a further explanation for the uninitiated, intraism is described as an art form which "draws on psychedelic thought and seeks the art description of the structural facts science, biology and medicine collate for us, concerning the regions within the body surface, within its substance and within its tracts, channels and impouchings".

Suitably motivated readers of *Nature* can now proceed to buy their canvasses and clean their brushes.

Naming Planetoids

THREE minor planets recently discovered by the Crimean astrophysical observatory have been named Dobrovolskii, Volkov and Patsaev, after the cosmonauts who perished in the Soyuz-11 disaster. This breach of the nomenclature rule that planetoids in the belt between Mars and Jupiter should bear feminine names is extremely rare for Soviet-named planetoids. Even so eminent a

personage as Tsiolkovskii required a change of gender before being commemorated as "Tsiolkovskaya", and planetoid 852, the first discovery of the Soviet era, commemorates Vladimir I. Lenin in the feminine guise of "Vladilena".

Since the Revolution, Soviet planetary nomenclature has been under the control of Professor Natal'ya Sergeevna Yakhontova, a pioneer of equal rights for women in astronomy.

Predicting Population

MANY people have come to grief in trying to make predictions of the future population. One of the chief problems is that fertility is most quixotic and it is not possible to tell in advance how this is going to change. As an example, nine months after the great blackout on the eastern seaboard of the United States in 1967 there was an unprecedented increase in the birth rate which made nonsense of all predictions.

What chance is there that the birth rate in Britain in 1974 will register an increase? In 1972 the rate was 14.9 per thousand of the population compared with 16.2 in 1971. Television, it must be remembered, went off the air at 10.30 p.m. from December 17 onwards. In contrast to the situation in the United States in 1967, this will not happen for one night only in Britain. So, look out all maternity units from next September on.

Supersonics 1,000,000—Cloth Caps 0

THE British parliament was last week assured that the Concorde development programme would not be impeded by fuel shortages. Rather over a million gallons of fuel will be needed for Concorde in the next six months, but this is only 0.7% of total aviation fuel requirements.

On the other hand, in the same week the government could see no way that the few British soccer clubs who have bought petrol generators could be allowed to use them for floodlighting grounds. Re-timed fixtures will, at a guess, prevent a hundred thousand from attending each week. A generator uses 20 gallons during a game.

Reverse Energy

Two weeks ago we reported on research in progress in Britain on synthesising gas from coal with the same burning characteristics as natural gas (*Nature*, **246**, 326; 1973).

This week we have been searching for evidence of some research in progress on converters of natural gas into coal. Unfortunately there does not seem to be any going on—at least in Britain.

NEWS AND VIEWS

Wanted—A Taxonomist for Magnetism

UNTIL quite recently, magnetism was a nice, tidy branch of physics. Every student of the field knew that it was neatly divided into diamagnetism, paramagnetism, ferromagnetism, ferrimagnetism and antiferromagnetism: Néel was in his haven and all was right with the world. Such a sense of tidiness is apt to precede a thoroughgoing shakeup, and magnetism has been no exception. Now there is mictomagnetism, (crystalline) superparamagnetism, amorphous antiferromagnetism and, as the most recent candidate, speromagnetism. What this amounts to is that magnetism has come face to face with the physics of randomness, and randomness has turned out to be more subtle than mere regularity.

'Speromagnetism' is a term coined by Coey of Grenoble and Readman of Edinburgh in their letter on page 476 of this issue of *Nature*. They report on an examination of a natural gel consisting of hydrated amorphous ferric hydroxide in an organic matrix. The magnetisation curve at low temperatures shows a remanence, which indicates that there must be some kind of ordered magnetic structure. Combining magnetisation studies with a detailed examination by Mössbauer spectroscopy, the authors conclude that below 10 K the spins are coupled and locked within small particles of the order of 10 nm in size; above 10 K these particles become 'unblocked' and behave superparamagnetically—that is, the particles are now magnetically independent but in each the spins are still fixed in the absence of a constraining field. Only above 100 K does the material become a self-respecting paramagnet, with thermally randomised spins.

Applying Langevin theory to the superparamagnetic magnetisation curve leads to a net moment of $73 \mu_B$ per particle, and also to an estimate of the particle size as equivalent to 635 formula units of the hydrated ferric hydroxide. This at once poses a paradox, because $73 \mu_B$ for 635 formula units is consistent neither with ferromagnetic nor with antiferromagnetic coupling within a particle. The authors are driven to the conclusion that

the spins are arranged effectively at random. The point to notice is that a purely random array of N spins of moment m in an independent small particle has a resultant moment of $\sqrt{Nm}$: this is simply the random walk equation, familiar from diffusion theory. Although the authors do not trouble to spell it out, the resultant saturation magnetisation is much greater for a population of spins distributed in many minute particles than for the same population arranged in a few large particles.

The authors call the behaviour of an array of small particles with fixed but random spins, which have an appreciable resultant moment only because of the small size of the array, by the name speromagnetism, from a Greek root meaning 'to scatter'. The interesting question is 'why an array of ferric spins is arranged randomly in spite of the undoubted presence of some antiferromagnetic nearest-neighbour interactions, and on this they are able only to speculate. It seems that the existence of variable exchange interactions in an irregular structure must in some way be held responsible.

This intriguing paper links with a substantial body of recent research concerned with the magnetic properties of extensive (rather than particulate) amorphous materials, dignified this year with a full-scale volume of conference proceedings (*Amorphous Magnetism*, edited by H. O. Hooper and A. M. de Graaf, Plenum, New York). Both ferromagnetic and (even more surprisingly) antiferromagnetic characteristics have been observed in alloy glasses. The theory of spin assemblies where the strength and even the sign of exchange interaction vary according to the spacing of randomly packed neighbours is very complex and has only recently been attempted. The new phenomenon of speromagnetism (or amorphous superparamagnetism) adds a further delectable layer of complexity to what is already a highly elaborate network of phenomena. Truly the services of a magnetic taxonomist will soon be needed to bring order out of the amorphous multiplicity of concepts.

R. W. C.

Prospects for Hepatitis B Vaccines

DISCUSSIONS on active immunisation against hepatitis B infection centre around the work of Krugman and his associates at the Willowbrook State School who use as the 'vaccine' a known infective human serum (MS-2 serum) that contains hepatitis B antigen and which is diluted 1 in 10 and boiled for 1 minute (Krugman *et al.*, *New Engl. J. Med.*, **288**, 755; 1973). This heat-inactivated serum is not infective and it successfully prevented or modified hepatitis B in twenty (69%) of twenty-nine children who were challenged after 4 to 8 months with serum containing the MS-2 strain of hepatitis B virus. The illness in the remaining nine children was generally mild, with jaundice occurring in one child. Abnormal levels of serum glutamic oxaloacetic transaminase were noted in twelve (41%) of the twenty-nine children. Hepatitis B antigen was detected in the serum of twelve children and the

antigen persisted in three of the twenty-nine children giving a chronic carrier rate of about 10%; whereas in a control group of twenty-four non-immunised children a chronic carrier rate of 37.5% was observed after exposure to MS-2 serum. Hepatitis B antibody, assayed by sensitive techniques, was induced in eight of twenty-nine children, but it was transient in six of the children and furthermore one of the children with 'vaccine'-induced antibody became a persistent carrier of the antigen after challenge. The results with the heat-inactivated serum were essentially the same after one, two or three inoculations.

Diluted and heat-treated whole serum may be regarded as an inactivated 'vaccine' but it is a crude way of inducing immunity and it is unlikely that such material will be licensed for general use. The repeated failure consistently to grow hepatitis B virus in tissue or organ cultures has

hampered progress towards the development of a safe and effective vaccine. Attention has therefore been directed more recently towards the use of other preparations for active immunisation against type B viral hepatitis.

The close association between hepatitis B antigen and human hepatitis B virus is firmly established (*Bull. Wld Hlth Org.*, **42**, 957; 1970). The morphology of hepatitis B antigen shares a number of features with known viral structure. The principal antigenic constituent is a rather pleomorphic spherical particle measuring about 20 nm in diameter but with a range of 16–25 nm. The presence of tubular forms, with an average diameter of 20 nm and often several hundred nanometres in length, is a characteristic feature. The third type of particle (Dane particle) is also spheroidal, measuring about 42 nm in diameter, with an inner core of about 28 nm in diameter, a 2 nm shell and an outer coat about 7 nm in thickness. After detergent treatment of pellets of hepatitis B antigen obtained by ultracentrifugation of whole serum, the large 42 nm spherical particles separate into an outer coat of antigen and an inner component which is 27 nm in diameter (Almeida *et al.*, *Lancet*, ii, 1225; 1971). The inner component resembles morphologically a rhinovirus. Almeida *et al.* found that antibody present in the serum of patients after recovery from type B hepatitis reacted with the inner component, but not with the outer hepatitis B antigen component, to yield immune aggregates resembling those seen in homogenates of liver taken post-mortem from patients with hepatitis B. Antibody to the inner core was absent from the pre-hepatitis sera from the same convalescent patients. It was suggested that antibody to hepatitis B antigen develops during the course of the infection, but that it is subsequently cleared from the serum with clinical improvement, while a normal immune response is produced to the inner core of the 42 nm particle. These findings have since been confirmed (Barker *et al.*, *J. infect. Dis.*, **127**, 648; 1973; and Hofnagle *et al.*, *Lancet*, ii, 869; 1973) and lend support to the view that the inner component may indeed represent the infectious agent of type B hepatitis, although final confirmation must await the successful cultivation of the infectious agent.

It is uncertain whether hepatitis B antigen represents incomplete virus particles, aggregates of protein subunits, excess virus-coat material, overproduction of unstable virus-like particles or a modified cellular component whose synthesis is specified or specifically derepressed by the hepatitis B virus. But it seems likely that the antigen consists principally of excess viral coat proteins coded by the infecting virus. Isolated viral coat protein challenges the body's immune mechanism in the same way as the whole infectious agent and the possibility of using purified hepatitis B antigen particles, which are free of nucleic acid and therefore of infectivity, seems attractive. Such an approach, however, is precluded by the amounts of host protein that may be complexed with the viral protein in quantities which are far in excess of the protein coat of most recognised viruses. These host proteins may include various pre-existing structures of the liver cell (Popper and MacKay, *Lancet*, i, 1161; 1972) and may thus induce undesirable immunological reactions. Subunits of the antigen, in the form of small polypeptides, on the other hand, offer a much more attractive proposition as immunogens, although it remains to be determined whether antibody to hepatitis B antigen, to the inner core or to other components is responsible for protection against infection.

Subunit Hepatitis B Vaccine

Hepatitis B antigen was recently fractionated by isopycnic centrifugation in a continuous linear gradient of caesium chloride followed by rate sedimentation separation (Vyas *et al.*, *J. Immunol.*, **108**, 1114; 1972). The rate sedimentation procedure resolved the material into three protein peaks containing the small spherical, tubular forms and the 42 nm (Dane) particles of the antigen respectively. Amino acid analysis of the first peak revealed that the protein seems to consist of two subunits and it contains a high proportion of proline, leucine and serine and a low content of tyrosine.

In another study, Dreesman and colleagues considered some of the biophysical and biochemical properties of hepatitis B antigen in plasma collected from three patients with anicteric hepatitis. The original samples were found by electron microscopy to contain the small spherical 20 nm particles, tubular forms and 42 nm particles. High speed centrifugation yielded pellets which were treated at pH 2.4 before further purification by isopycnic and rate zonal centrifugation. Electron microscopic examination of the pelleted particles after low pH treatment disclosed that both the large 42 nm particles and tubular forms were lost, yielding a preparation containing a mixture of spherical particles with a diameter of 19 ± 2 nm and a population of larger particles measuring 25 ± 2 nm in diameter. The relative proportions of the 19 nm and 25 nm particles were dependent on the original plasma. In one plasma, in which relatively few 42 nm particles were found in the starting material, 90% of the purified particles had a diameter of 19 nm. A plasma rich in 42 nm particles, however, yielded a purified preparation containing 65% of 25 nm particles, which may represent the core material of the 42 nm particles. The difference in size was confirmed by the presence of two distinct populations with average molecular weights, calculated from high speed equilibrium data, of 3.6×10^6 and 4.5×10^6 .

There were no significant differences in the amino acid composition of antigen purified from the plasma of the three patients. A comparison of the amino acid composition of hepatitis B antigen with that of adenovirus type 2, poliovirus, herpes virus and KB cells revealed that the antigen is distinctive in having significantly higher levels of cysteine (or cystine), proline, leucine and phenylalanine and lower levels of both the acidic and basic amino acids lysine, arginine, aspartic acid and glutamic acid. A relatively low concentration of tyrosine and histidine was found.

Six iodinated polypeptides were identified in purified hepatitis B antigen preparations by disk polyacrylamide gel electrophoresis in sodium dodecyl sulphate-urea gels (Dreesman *et al.*, *J. Virol.*, **10**, 469; 1972). The three large polypeptides had molecular weights of 39,000, 32,000 and 27,000 respectively and the three smaller polypeptides had molecular weights of 22,000, 16,000 and approximately 10,000 respectively.

The close association of hepatitis B antigen with normal serum components has been an acknowledged difficulty in developing centrifugation techniques for separation of the antigen in pure form from serum. Since there is almost complete recovery of total protein after separation by electrofocusing, this technique was applied for the purification of hepatitis B antigen (Howard and Zuckerman, *J. gen. Virol.*, **20**, 253; 1973). Antigenic activity was found in those bands of serum proteins which possessed isoelectric points over the pH range 4.0 to 7.0. Antigenic

activity was not detected in association with separated gamma globulins, which is in accord with the long epidemiological and clinical experience that gamma globulin is free of the risk of transmitting hepatitis and with the failure to detect hepatitis B antigen, a marker associated with infectivity, by electron microscopy after Cohn fractionation of human plasma known to contain the antigen (Zuckerman *et al.*, *J. clin. Path.*, **24**, 2; 1971). The major portion of serum proteins was removed by gel filtration on Sephadex G200, concentrated, and hepatitis B antigen separated from the remaining unwanted serum protein by isoelectric focusing in a sucrose gradient containing carrier ampholytes (Ampholine) at a final concentration of 1%. Hepatitis B antigen was found to focus in two discrete bands (Howard and Zuckerman, 1973) with isoelectric points 3.65 and 4.33 for the *ad* subtype and 3.95 and 4.90 for the *ay* subtype (Howard and Zuckerman in *Isoelectric Focusing* (ed. by Arbutnot), Butterworth, in the press). Normal serum proteins were not detected in the two bands. It is also interesting to note the similarity of behaviour of the antigen to some plant viruses focused in polyacrylamide gels (Rice and Horst, *Virology*, **49**, 602; 1972).

The apoprotein constituent of hepatitis B antigen was found to be organised into a number of definable polypeptides. Aliquots from peaks I and II of separated antigen activity were solubilised and the resulting protein solution was then subjected to electrophoresis in 10% polyacrylamide gels. After staining with Coomassie Brilliant Blue, eight identical polypeptides were discernible preparations from both peaks. The range of molecular weights was approximately 10,000 to 300,000. Densitometry of the stained gels revealed that at least one polypeptide (MW 100,000) was a major component of the first peak, but it was present in a small quantity only in the second peak. Selective degradation experiments suggest that this polypeptide is a part of the surface structure of the antigen (Howard and Zuckerman, in the press). Analysis of antigen bearing the *ay* subdeterminants by the same technique has not yet been completed.

Such polypeptide preparations should be investigated as potential vaccines for hepatitis B by defining the immunogenic moiety by studies in appropriate nonhuman primates.

Synthetic Hepatitis B Vaccine

An immunochemical study of purified hepatitis B antigen is essential for understanding this unique antigen. Analogous to the TMVP decapeptide, the primary sequence of the haptenic peptide of hepatitis B antigen may provide another approach for a development of a synthetic peptide, which when coupled to a macromolecular carrier could serve as a suitable immunogen. Once detailed data are available on the protein, peptide and amino acid composition of this antigen, it should be possible to define by animal immunisation the moiety responsible for the antigenic activity.

There are reports in the literature to support the feasibility of such an approach. For example, in 1966 Stewart *et al.* (*Biochemistry*, **5**, 3396; 1966) defined the antigenic moiety of TMV protein decapeptide. Arnon and her colleagues (*Proc. natn. Acad. Sci., U.S.A.*, **68**, 1450; 1971) showed that it was possible to use a synthetic macromolecule for eliciting antibodies reacting exclusively with a specific region of a native egg-white lysozyme. This

was achieved by synthesising a particular segment of the enzyme from its amino acid components, attaching the peptide to a synthetic polypeptide carrier and using the conjugate for immunisation. The resulting antibodies reacted with native lysozyme in a unique, conformation-dependent antigenic determinant. Of course, in the case of lysozyme both the amino acid sequence and the three-dimensional structure are known, and the synthesised peptide was designed on the basis of previous information concerning its contribution to the antigenic specificity of the molecule.

A similar approach might be attempted for type B hepatitis, depending largely on the success in elucidating the structure of hepatitis B antigen, since there is little doubt that polypeptides and other moieties such as specific lipoproteins can be attached to a macromolecular carrier (Sela, *Adv. Immunol.*, **5**, 29; 1966) for subsequent immunisation. The prospects of active immunisation against hepatitis B appear brighter.

A. J. Z. and C. R. H.

Origin of Marginal Seas

WITHIN the framework of seafloor spreading and plate tectonics the origin of marginal ocean basins is still something of an enigma. Thus the geological evolution of the Mediterranean, the Gulf of Mexico and the various marginal seas of the northwestern Pacific is currently hotly debated. The evolution of the main ocean basins within the past 60–70 million years is discernible in remarkable detail as a result of the bathymetric expression and magnetic record of spreading about mid-ocean ridge crests. Even details of the geometry and timing of shifts of a spreading centre can be documented for this period of time. The age of older oceanic crust is less readily determined partly because the bathymetric expression has decayed and there are long periods of time during which the Earth's magnetic field did not reverse its polarity, but also because subsequent igneous activity may complicate both the bathymetric and magnetic signatures. Nevertheless the details of Mesozoic ocean floor spreading are gradually emerging and if unexpected in detail are certainly not unexpected in terms of basic principles. With regard to marginal basins, however, basic principles are at stake; some geologists seriously doubt whether these areas, even where they attain oceanic depths, are floored by oceanic crust formed by spreading about a mid-ocean ridge crest.

Many of the marginal seas are bounded wholly or in part by subduction zones (that is, active mountain belts or island arcs) and the origin or initiation of these zones, both in space and time, is fundamental to a clear understanding of the seas themselves. In contrast to mid-ocean ridge crests, whose position relative to continental margins during the past 100–200 m.y. is often well known, the position of the destructional plate margins in the past is much less obvious. If one looks at a present day world map it is tempting to assume that subduction zones either form at continental margins, to produce an Andean-type situation, or at some distance from the margin, and presumably within oceanic crust formed by spreading, to form the island arcs and marginal basins of the western Pacific. In this latter case crust older than the arc itself

would be isolated behind it. This is one possible mode of origin for the West Philippine Sea, which is discussed on page 458 of this issue. If, however, a subduction zone forms at some distance from a continental margin and dips away from it, the zone will ultimately collide with the margin, as a result of the destruction or resorption of the intervening oceanic crust, and the polarity of the subduction zone is presumably reversed to produce, finally, an Andean-type margin. This process has sometimes been referred to as 'Benioff-plane reversal'. Conversely a subduction zone which forms at or near to a continental margin, and dips beneath it, may subsequently be rafted away from it by a process of 'back-arc spreading'; that is, the formation of a small ocean basin behind the arc by a process analogous, perhaps equivalent, to spreading about a mid-ocean ridge crest. Clearly such a process would mean that the back-arc basin would be floored by crust which is younger than the arc itself.

The first person to suggest the process of 'back-arc spreading' was Karig (*J. geophys. Res.*, **75**, 239; 1970) and he documented it primarily in terms of the sediment thickness and near-surface structure revealed by seismic reflection profiling. He envisaged it as an episodic process with phases of spreading occurring immediately behind the arc and producing basins separated by ridges of former island-arc material and younging towards the arc. This then was Karig's model for the origin of the western Pacific basins, including the Philippine Sea, the largest of the back-arc basins. It is only fair to say that much of the geophysical and geological data (which includes deep-sea drilling results) obtained since the time of Karig's initial suggestion have tended to corroborate his ideas, and his model is now widely accepted.

Precisely a year ago, however, in this journal (*Nature*, **240**, 453; 1972) Ben-Avraham *et al.* made a case for the existence of an extinct spreading centre in the West Philippine Sea, the spreading axis of which trends NW-SE and the age of which probably exceeds that of the Mariana island arc to the east. They felt therefore that it was more compatible with formation in the main Pacific basin prior to the formation of the arc than with the concept of back-arc spreading. In this issue Karig *et al.* present a rejoinder armed with new data acquired as a

result of Deep-Sea Drilling Project leg 31 in the Philippine Sea. They maintain that it was quite fortuitous that the single bathymetric and gravity profile across the 'Philippine Ridge', of Ben-Avraham *et al.*, seems to be consistent with the model of an extinct spreading centre. Further work, they claim, favours the original interpretation of the feature by Hess (*Bull. Geol. Soc. Amer.*, **59**, 417; 1948) as a strike-slip fault. Although the interpretation of Ben-Avraham *et al.* was in many ways convincing, its greatest weakness was the paucity of data on which it was based, essentially little more than one profile. Also the relief of the central rift area is somewhat excessive and more reminiscent of present day transform faults than ridge crests. The symmetrical magnetic anomalies were the most convincing evidence put forward, but a worrying aspect of these was that they were interpreted as reflecting reversals during late Mesozoic time when from other areas and palaeomagnetic studies

there are strong indications that the Earth's magnetic field was of a single, normal, polarity for much of the time.

In spite of the fact that Karig *et al.* feel that their new data invalidate the interpretation of the central basin feature as a ridge rather than a fault, they admit that they are unable as yet to provide an unequivocal answer to the origin of the West Philippine Basin. Many questions remain unanswered not least of which is the extent and role of Tertiary volcanism which significantly post-dates the origin of the crust, and the occurrence of non-calcareous basal sediments in some areas which on the face of it argues against formation at an elevated spreading centre. It is clear that the nature and origin of marginal seas is going to be a battlefield for earth scientists for some time to come; a battlefield which may ultimately become a legal and political one in view of the potential economic importance of marginal basin geology.

From a Correspondent

RIBOSOMAL RNA

Mechanism of Amplification

from a Correspondent

RIBOSOMAL gene amplification during oogenesis in *Xenopus* (Gall, *Proc. natn. Acad. Sci. U.S.A.*, **60**, 553; 1967) suggested the possibility that a similar mechanism of specific gene amplification acts during the differentiation of cells to produce large quantities of a single or a few types of protein. In this way anything learnt about the mechanism of rDNA amplification might have a wider and more important impact on developmental biology. Two recent tests of this idea, however, one for silk fibroin synthesis in the silk gland of the moth *Cecropia* (Suzuki, Gage and Brown, *J. molec. Biol.*, **70**, 639; 1972) and one for globin synthesis in differentiating blood cells (Bishop, Pemberton and Baglioni, *Nature new Biol.*, **235**, 231; 1972), have shown that specific gene amplification during differentiation is not a general phenomenon.

In spite of this apparent relegation of ribosomal gene amplification to the level of biological oddity, it has continued to excite interest on four counts. Intriguing and novel molecular mechanisms may be involved (see Tocchini-Valentini and Crippa, *Proc. natn. Acad. Sci. U.S.A.*, **68**, 2769; 1971); it may be related to important features of the maintenance and evolution of multiple gene loci (Buongiorno-Nardelli, Amaldi and Iava-Sanchez, *Nature*, **238**, 134; 1972);

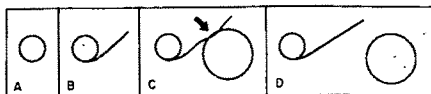
Amaldi *et al.*, *Nature*, **242**, 615; 1973); the nature of dosage compensation both in rRNA synthesis and rDNA amplification observed in heterozygote (+/nu-) animals (Macgregor, *Nature new Biol.*, **246**, 81; 1973) and of the 'dominance' phenomena found in interspecies crosses (*Nature*, **246**, 60; 1973) may tell something of the mechanisms controlling rRNA synthesis and rDNA amplification.

Rolling Circle Intermediate

Recent work by Hourcade, Dressler and Wolfson (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 2926; 1973) provides convincing evidence that rDNA amplification proceeds by way of a rolling circle intermediate. What they have done is to isolate by CsCl density gradient centrifugation rDNA from amplifying ovaries, taking great care to avoid shearing forces which might cause breakage of DNA molecules. They looked at this DNA with an electron microscope and found that although most molecules are linear, 2-5% are circles—and rolling circles (circles with tails) which range in size from 8-140 × 10⁶ daltons. By measuring contour lengths, they were able to show that most of the circles with a mass of less than 40 × 10⁶ daltons fall into discrete size classes corres-

ponding to multiples of the basic repeating unit (mass 8×10^6 daltons) found in rDNA. They suggest that the reason why larger circles do not is that the error in measurement causes overlap of neighbouring size classes.

Circles outnumber rolling circles by six to one, but rolling circles also fall into the same multiple series of the basic ribosomal gene. It might be argued that the tail on these rolling circles was originally inserted on the circle at both ends to give a θ -shaped Cairns type replicative form and that one end has been liberated by breakage during isolation. Breakage of a Cairns form would always give tails shorter than the circles and presumably also circles with two tails; in fact 85% of tails are longer than the circle to which they are attached and moreover no circles with two tails were observed.



Hourcade *et al.*'s idea of how a rolling circle intermediate is expected to produce, by a recombination event in its tail, multimer-length amplified DNA circles. This recombination event could also occur if the tail has been detached from the rolling circle and exists as an intracellular concatemer. Single line represents a DNA double helix.

Hourcade, Dressler and Wolfson also saw two other DNA forms, a Y-shaped structure with three unequal arms which may be produced by breakage within a rolling circle, and more important, two θ -shaped Cairns forms, which may indicate that both rolling circle and double rolling circle or Cairns type replication proceed together or that one precedes the other during amplification.

Since rolling circles represent such a small proportion of all molecules, it may be that they represent a minor non-rDNA component with the same buoyant density and same basic repeat length as rDNA. Hourcade *et al.* used the technique, originally applied by Brown, Wensink and Jordan (*J. molec. Biol.*, **63**, 57; 1972), of partial denaturation of DNA by heat, alkali or formamide, followed by electron microscopy to map denatured and native regions. As expected they found that the same denaturation pattern exists in linear molecules, circles and rolling circles proving their sequence identity.

Similar work by Bird, Rochaix and Bakken (*Molecular Cytogenetics*, Oak Ridge Symposium, 1973) confirms the presence of rolling circles in rDNA from amplifying ovaries. They have also used tritiated thymidine to label replicating DNA followed by autoradiography in the electron microscope which allows them to select rapidly for replicating molecules (those which have

silver grains over them). It turns out that grains are seen over rolling circles, providing evidence that the rolling circles observed really are synthesising DNA.

Other Mechanisms

Other molecular mechanisms for rDNA amplification have been proposed. Buongiorno-Nardelli *et al.*, from a study of a large number of amphibian species, provide evidence for a $2n$ relationship between the number of ribosomal genes per diploid cell (R) in different species, and also that a similar $2n$ series exists for the total number of amplified oocyte nucleoli (A) in these same species. They found three cases in which $R=A$ while there were nineteen cases in which $R>A$ and none where $R<A$. To account for these observations they proposed that amplification proceeds by the following mechanism; an initial series of crossover events release each rRNA gene as a monogenic circle, there are thus R circles, these circles replicate by the double rolling circle mechanism; characteristic of the replication of λ phage in *Escherichia coli*, giving rise after n rounds of replication to circles with $2n$ genes. Thus R is equal to or greater than A , depending on whether all the genes are liberated or whether they are liberated as multiples of the repeat unit, but R is never less than A . The single rolling circles observed by Hourcade *et al.* and, more important, the arithmetic rather than geometric increase in the size of circles, argues specifically against the Buongiorno-Nardelli model for amplification although not against their general conclusions about its possible significance as a correction mechanism for multiple gene loci.

Tocchini-Valentini and Crippa (*Proc. natn. Acad. Sci. U.S.A.*, **68**, 2769; 1971) suggested that rDNA amplification might proceed by way of the synthesis of DNA by a reverse transcriptase on an initial complete RNA transcript of the ribosomal gene repeat unit. They provided evidence for the presence in amplifying ovaries of *Xenopus* of such an RNA transcript which is much larger (47S) than the normal rRNA (40S) precursor and also contains sequences complementary to rDNA. The presence of an RNase resistant RNA-DNA complex containing high molecular weight RNA was predicted and found. A rifampicin derivative, which inhibits viral reverse transcriptase, was also found to inhibit rDNA amplification but not main bond DNA synthesis. These observations taken together seemed convincing enough; however, Bird, Rogers and Birnstiel (*Nature*, **242**, 226; 1973), using techniques of greater refinement and sophistication, were unable to verify any single one of them and concluded that reverse transcription

is an unlikely solution to the problem of the amplification mechanism. The rolling circle DNA forms seen by Hourcade *et al.* and Bird *et al.* add further weight to the evidence against reverse transcription as the major molecular mechanism for rDNA amplification but do not exclude its operation early in amplification or at a low level throughout amplification.

Origin of rDNA Circle

Several questions remain unexplained by existing work, the main one being the origin of the initial rDNA circle, which may formally be derived in four ways. One is by maternal inheritance as an episome (Wallace, Murray and Langridge, *Nature new Biol.*, **230**, 201; 1971) and has been disproved by the demonstration of the lack of maternal inheritance for rDNA amplification in *Xenopus laevis-mulleri* hybrids (Brown and Blackler, *J. molec. Biol.*, **63**, 75; 1972). Second, an RNA transcript may give rise by reverse transcription to a DNA molecule which is circularised by a DNA ligase and then replicates by the rolling circle, double rolling circle or Cairns type intermediates. The attraction of this model is that it eliminates the need to postulate production of rDNA circles by crossing over within the gene cluster. Third, crossing over within the rDNA cluster might generate all sizes of circles from single genes to the complete locus. The fourth possibility is semiconservative DNA replication of a part or the whole of the rDNA locus following by excision at growing points and circularisation with ligase or crossing over. A corollary of this question is whether representatives of all chromosomal rRNA gene sequences are present in amplified rDNA.

HORMONES

Binding to Receptor

from a Correspondent

STUDIES with rat ventral prostate have shown that androgen-sensitive tissues contain receptor proteins which interact with the androgen, and in the case of the naturally occurring hormone testosterone, its reduction to 5α -dihydrotestosterone is an initial and essential step in the interaction. Knowledge of the extent to which 5α -reductase and the receptor protein occur in tissues and of the ability of other potent steroidal androgens, which are not converted to 5α -dihydrosteroids, to interact with the receptor is limited. These aspects have been investigated in two recent contributions.

One might expect a close functional relationship between the receptor and enzyme proteins. Mainwaring and Mangan (*J. Endocr.* **50**, 121; 1973)

measured the concentration of receptor protein and 5α -reductase activity in the accessory sex glands from four species, rat, mouse, guinea pig and rabbit, and also in a number of other tissues which might be expected to contain the receptor, for example, muscle, because of the anabolic effect of the androgens, kidney tissue and mouse tumours which require androgens for growth. Binding activity was present in rat and mouse testes, mouse kidney, although this tissue seemed to take up testosterone as well as 5α -dihydrotestosterone, and significant nuclear binding of radioactivity was demonstrated in androgen-dependent but not in androgen-independent tumours in mice. With the exception of the levator ani muscle of the guinea pig, the binding and reductase activity in other muscles from the four species were small.

Although high activities of the 5α -reductase were found in the prostate and epididymis of the rat and mouse with smaller activities in seminal vesicles and kidneys, the testes and muscles investigated contained negligible activity. Surprisingly, rabbit prostate contained only about half the amount of receptor protein as rat prostate and 5α -reductase activity was virtually absent. These findings therefore show considerable variability in androgen-sensitive tissues from various species both in their concentration of receptor protein and their ability to convert testosterone to 5α -dihydrotestosterone.

Liao *et al.* (*J. biol. Chem.*, 248, 6154; 1973) studied the ability of natural and synthetic androgens to compete with 5α -dihydrotestosterone for binding to the cytoplasmic receptor protein and for retention by prostatic cell nuclei. There was a good correlation between the relative androgenicity of the synthetic steroids and their ability to compete with 5α -dihydrotestosterone for binding to the receptor protein and for retention by prostatic nuclei. Testosterone only competed slightly with 5α -dihydrotestosterone at the cytoplasmic level, however, although it did reduce retention of 5α -dihydrotestosterone at the nuclear level. Unlike testosterone which depends on reduction by 5α -reductase for its action, many synthetic androgens seem to bind directly to the receptor protein, without being reduced by 5α -reductase. The 17β -hydroxy group was essential for binding to the receptor protein and neither 17α -oxosteroids nor 17α -hydroxysteroids showed any significant binding.

From this study of a large number of steroids the authors conclude that the flatness of the steroid molecule around ring A is a determinant of the firmness of androgen binding to the receptor and that steric factors are more important in binding than the detailed electronic structure.

X-RAY SOURCES

Luminosity Function

from a Correspondent

RECENT investigations of the luminosity function and spatial distribution of the galactic X-ray sources are bringing astronomers nearer to an understanding of their origin. The distribution of a class of sources within our Galaxy can indicate an association with a known stellar population and hence give an idea of how they fit in with present ideas about stellar evolution. Dilworth, Maraschi and Reina (*Astron. Astrophys.*, 28, 71; 1973) and Margon and Ostriker (*Astrophys. J.*, 186, 91; 1973) conclude, in accord with earlier suggestions, that the galactic X-ray sources fall into at least two, and possibly three, distinct groups.

First, there are the sources populating the whole disk of the galaxy. These consist of two distinct types. There are the 'steady' sources, which have a wide spread of luminosities and among which a number have been identified with the remnants of supernovae; there are also

the 'highly variable' sources whose luminosities are all fairly close to 1.3×10^{37} ergs s^{-1} . The sources in this second subgroup are probably almost all associated with binary systems in which X-ray emission arises from accretion onto a compact object. Unresolved sources from this population could account for about half the galactic background emission.

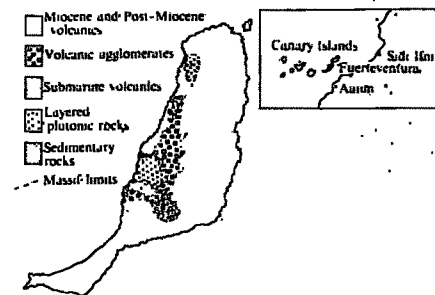
Second, there is a population of sources at the centre of the Galaxy. This population seems to consist of a single class of variable, high luminosity sources, with a relatively small spread in luminosity around 10^{38} ergs s^{-1} . This luminosity corresponds to the theoretical (Eddington) limit for the luminosity of an object with a mass about equal to that of the Sun. If the luminosity of such an object were much more than this, radiation pressure would exceed gravity in the surface layers and mass loss would ensue. This is not very compatible with the idea that accretion of matter is the process which powers the X-ray source. Thus it is comforting that on average the Eddington limit is not exceeded, and, looking ahead,

Upthrust Ocean Floor in the Canary Islands?

THE Betancuria massif, which forms the western part of the Island of Fuerteventura in the Canary Islands, has a core of layered gabbros, pyroxenites and peridotites associated with pillow lavas, siliceous and calcareous sediments and volcanic agglomerates. The whole is cut by a dyke swarm which is especially dense at the contact between the layered plutonic rocks and the other components of the formation, and was subsequently overflooded by three different basalt series ranging from Miocene to prehistoric. Finally, a carbonatite complex and syenitic and trachytic ring dykes and plugs were intruded.

Even on the basis of this superficial geological description there is a clear resemblance between the Betancuria massif and other ophiolite complexes such as the Troodos massif of Cyprus; and in *Nature Physical Science* last Monday (December 17) Gastesi proposes that Betancuria, like Troodos, is an uplifted segment of ancient oceanic crust (see figure). Of course, Gastesi's analysis is based on a much more detailed review of the geology than that just given, but the more rigorous examination strengthens the conclusion that all the units of the Betancuria massif are consistent with the ocean floor interpretation, and not just the plutonic rocks as proposed by Fúster *et al.* (Instituto Lucas Mallada, CSIC, Madrid, 1968). The principal differences between Betancuria and Troodos are chemical, the Betancuria rocks

being generally the more alkaline; but these do not appear to be serious enough to invalidate the basic conclusion.



Age data from the Betancuria massif are few and fail to give anything like a complete picture, although recent radiometric ages for the dykes lie in the range 46–28 million years. For the time being, therefore, Gastesi feels that two rather different patterns of evolution are possible. In the first, Betancuria was formed as part of the mid-Atlantic ridge, the radiometric ages representing "a more recent metamorphic episode in the development of the Atlantic margin". The second possibility is that the massif formed away from the mid-Atlantic ridge during the mid-Tertiary, perhaps as part of an abortive attempt to start a new ridge. Either way, what is now required is detailed geophysical work to discover how closely the structure and physical properties of Betancuria resemble those of the modern ocean floor.

Margon and Ostriker suggest that because of the small spread in luminosity about this limit, similar groups of X-ray sources in other galaxies could be used as 'standard candles', much in the same way as Cepheids have served till now.

Third, Dilworth, Maraschi and Reina argue that present observations do not rule out the possibility of a third class of low luminosity sources ($\sim 10^{38}$ ergs s^{-1}) which are at present indistinguishable from the isotropically distributed sources which are thought to be mostly extragalactic. This class cannot account for more than about 10% of these but could give rise to the rest of the galactic background emission.

PALAEOMAGNETISM

Past Secular Variation

from our Geomagnetism Correspondent

HISTORICALLY, palaeomagnetic data have been seen largely as indicators of the Earth's ancient dipole, rather than non-dipole, field. This is so whether they refer to the comparatively recent past, in which case the dipole orientation is given directly in terms of the Earth's geographic or geomagnetic coordinates, or to the more distant past, in which case the frame of reference is changed by continental drift and the dipole hypothesis appears as an assumption rather than as something to be determined directly from the data. In either case the scatter in measured palaeomagnetic directions arising from the effects of the much more rapidly varying non-dipole field is usually seen as an embarrassment, and is 'averaged out' mathematically from the results of a large number of rock samples.

But in recent years there has been a growing interest in the scatter itself, or rather in what useful information may be derived from what has traditionally been regarded as a nuisance. If the ancient non-dipole field introduces scatter or 'noise' into the palaeomagnetic dipole 'signal', the argument goes, it should be possible to work back from the scatter to determine the old non-dipole field. Unfortunately, the idea is more easily stated than put into practice because not all of the observed scatter is produced by the non-dipole field. Experimental error, local magnetic anomalies and dipole wobble may increase the scatter and incomplete sampling may either underestimate or overestimate it; and all these and other factors must be controlled or measured in order to assess what part of the scatter is truly due to the phenomenon under investigation.

Some of the difficulties involved are well illustrated in an attempt by Watkins (*J. geophys. Res.*, **78**, 7763; 1973) to determine the secular variation during

the Brunhes epoch using lava flows from Réunion Island in the Indian Ocean region. This is not the first time that Réunion rocks have been used for this purpose. A few years ago, Chamalaun (*J. geophys. Res.*, **73**, 4647; 1968) measured the palaeomagnetic directions of forty-nine Réunion lava flows, obtaining what Watkins *et al.* (*Geophys. J.*, **28**, 1; 1972) later calculated to be an angular standard deviation of about 20° in the virtual geomagnetic poles (VGP) with upper and lower confidence limits of 23.2° and 17.5° , respectively. But Chamalaun used an average of less than two samples per lava flow, and so his data could not be used to calculate, and hence remove the effects of, the within-lava variation. Cox (*Earth planet. Sci. Lett.*, **6**, 257; 1969) thus rejected the final result on the grounds that the sampling was inadequate to allow a true determination of the ancient secular variation; and the field was left open to a much more thorough investigation involving more intensive sampling.

By sampling at a level of at least six samples per lava flow, Watkins clearly hoped to be able to obtain a result which would overcome the objections of Cox and thus be accepted as a true estimate of the ancient secular variation. Accordingly he carefully collected and measured 160 cores which were restricted to the Brunhes epoch by the use of previous potassium-argon ages, field polarity measurements and known stratigraphy, and which were restricted to locations at which accurate orientation could be carried out with respect to known geographic bearings. For flows that did not have anomalous palaeomagnetic directions (three did), the angular standard deviation of the VGPs arising solely from secular variation (that is, after removing other contributions to scatter such as that due to within-flow variation) was 17.7° with upper and lower confidence limits of 22.8° and 14.4° , respectively—which is little lower than the standard deviation obtained by Chamalaun using less than two samples per flow and thus still much higher than that to be expected on the basis of the present field.

Taken at face value the new result seems valid enough. The range of known radiometric ages involved, for example, is about 0.4 million years or over half the length of the Brunhes epoch, suggesting that an adequate range of time has been sampled. On the other hand, if the Watkins result really is valid, its similarity to the Chamalaun result would imply that there is little to be gained by increasing the level of sampling to over six samples per flow. Although this is not impossible, it is intuitively unlikely and conflicts with some previous experience.

But what really throws doubt on the new result is the fact that the angular

SOLAR SYSTEM

Vulcan?

from a Correspondent

INSTRUMENTS aboard Skylab may detect an object moving in an orbit closer to the Sun than the planet Mercury, according to Henry Courten of Dowling College at Oakdale, New York. Courten has photographed the regions around the Sun regularly at total eclipses since 1966. During the 1970 eclipse in North America, one object was photographed near the Sun from three widely spaced observing sites. These images could be of a previously unknown member of the Solar System orbiting close to the Sun.

Courten believes a planetesimal "between 80 and 500 miles in diameter" moves in an orbit about 0.1 AU from the Sun. On his photographs, this appears as a star-like object between magnitude +7 and +9. Other images on Courten's plates indicate that a complete asteroid belt may exist between Mercury and the Sun.

Courten is a guest investigator on the Skylab white-light coronagraph experiment. "If intra-Mercurial, solar-orbiting objects exist, they will eventually pass through the coronagraph field of view", he says. The only problem is that the sensitivity of the Skylab instrument borders on the limit of brightness of Courten's photographic images.

dispersion supposedly due solely to ancient secular variation is significantly higher than that due to the present field, and is moreover, out of line with ancient dispersion results from other Indian Ocean islands such as the Comores Islands, the Crozet Islands and Amsterdam Island. This could, of course, be due to a regional secular variation anomaly, which affects Réunion but not the other islands. Watkins believes it more likely, however, that an insufficient number of separate lava flows have been sampled, notwithstanding the long time range. Although he took over six samples from each flow, the total number of flows involved was eighteen compared with Chamalaun's forty-nine. Normally, eighteen intensively sampled flows might be expected to yield a valid result where forty-nine poorly sampled flows might not; and indeed Watkins's new value may turn out to be correct. Unfortunately, the level of doubt is sufficient to require yet another investigation involving not only high density sampling but a much larger number of flows.

ZOOLOGY

Pogonophoran Phylogeny

from a Correspondent

THE first international symposium on Pogonophora, which took place in the University of Copenhagen on November 1-3, had as its main topic the evolution and phylogeny of the group, but the discussions covered all aspects of the biology of these enigmatic deep-water benthic invertebrates. The symposium was organised by A. Nørrevang, with financial assistance from the Danish Research Council.

On the first day there were informal discussions and demonstrations of material, including some live animals brought along from the Norwegian fjords by T. Brattegaard (University of Bergen Biological Station). The second day, under the chairmanship of J. B. Kirkegaard (University of Copenhagen), started with some very intriguing ideas of his colleague H. Lemche on the embryology and phylogeny of the main

invertebrate groups. E. B. Cutler (University of Syracuse, Utica) then reviewed the occurrence of supposed protostomian and deuterostomian characters in Pogonophora and suggested that the group should be regarded as related to forms ancestral to both of these major subdivisions of the Eumetazoa. J. van der Land (University of Leiden) and A. Nørrevang reported on the morphology of a newly discovered Atlantic species of *Lamellibrachia* and suggested that this genus might be regarded as a subgroup of the Annelida. M. Webb (University of Durban, Westville) provided a thorough account of the excretory and genital systems of the Pacific species of *Lamellibrachia*, which he preferred to continue to regard as aberrant pogonophores. T. Bakke (University of Bergen Biological Station) briefly described the important early stages in the development of the artificially fertilised egg of *Siboglinum*; the cleavage could not be regarded as either spiral or radial.

At this stage in the session R. Siewing (University of Kiel) read a translation of a letter from A. V. Ivanov (Zoological Institute, USSR Academy of Sciences, Leningrad) regretting that he was prevented from attending, and announcing the discovery of some new facts on gastrulation in *Siboglinum*. E. Southward (Marine Biological Association, Plymouth) discussed the fine structure of the recently-discovered segmented and setate hind-end of *Siboglinum*, and traced its origin from the posterior segment of the larva, comparing the number of annelid characters and more general characters thus revealed. B. L. Gupta (University of Cambridge) and C. Little (University of Bristol) provided a far reaching and comprehensive account of many aspects of the fine structure of Pogonophora in comparison with other invertebrates, and pointed out the pitfalls awaiting the investigator trying to deduce relationships from functional morphology: Gupta finally expressed a doubt that pogonophores are coelomate animals at all. A. J. Southward (Marine Biological Association, Plymouth) summarised what had been found out or deduced about the feeding of these free-living yet gutless animals, and stressed the phylogenetic problems involved in the evolution of an epidermal mechanism of food absorption; he wondered what environmental conditions and selective pressure could lead to the loss of an existing internal digestive system.

Brattegaard then analysed the fauna associated with pogonophores, especially in the fjords; there seemed to be no consistent relationship between a pogonophore species and a single benthic community, though the organic content of the habitat seemed to be important as were abiotic factors such as temperature and particle size of the sediment.

The third day of the meeting, under the chairmanship of C. Nielsen (Marine Biological Laboratory, Elsinore), opened with some ideas of Siewing on phylogeny in relation to embryology and development of the coelomic cavity: the Pogonophora were placed well down the phylogenetic tree, close to the origin of the archicoelomates (Echinodermata and Lophophoria), with the Spiralia (for example, Annelida, Arthropoda) regarded as an offshoot of the main line of development.

At the final dinner, held at the Zoological Museum, Nørrevang was able to read the full abstract of Ivanov's intended paper, just delivered by express post. This confirmed a reassessment of the embryology of the group, no longer regarded as having radial cleavage, and it was suggested that Pogonophora form a separate group of the Eumetazoa, distinct from the Protostomia and Deuterostomia.

INSECTICIDES

Knockdown and Kill

from a Correspondent

NATURAL pyrethrins have been used extensively as insecticides partly because of their toxic properties but principally because of their rapidity of action—effects are observable in minutes against hours for chlorinated hydrocarbons. Doses applied topically cause uncoordination leading to knockdown of flies, mosquitoes and cockroaches. High doses cause death but at lower levels there may be recovery although this is usually prevented by the addition of a synergist such as piperonyl butoxide.

The advent of synthetic pyrethroids has stimulated further study into structure/activity relationships as these substances can occur as optical and geometrical isomers. 'Knockdown' was the subject of a symposium organised by the Biophysical and Physiochemical Panel of the Pesticides Group, Society of Chemical Industry, held on November 23.

P. E. Burt (Rothamsted Experimental Station) discussed the possibility of knockdown and kill being associated with different sites of action; in his view both actions are on the central nervous system and the peripheral nerves are not involved. This view was also taken by M. G. Ford (Portsmouth College of Technology) from a study of doses applied topically on the desert locust. A logarithmic plot of the time of 50% response against weight of applied dose gave linear relationships for kill and knockdown using the synthetic pyrethroids bioallethrin and bioresmethrin.

M. Elliot (Rothamsted Experimental

Station) discussed various synthetic pyrethroids in relation to knockdown and kill. Compounds with good knockdown are usually relatively poor as killing agents but their rapid action is probably due to a higher polarity which facilitates rapid penetration of the insect cuticle. Knockdown can be correlated with polarity, which is related to R_F values measured in appropriate chromatography systems.

J. Lhoste (Procida, Paris) related speed of knockdown of mosquitoes (*Aedes aegypti*) with the stereochemical structure of eight allethrin isomers. Test compounds were applied to a flat 'mosquito' coil of suitable composition, which burns slowly volatilising a substantial proportion of the insecticide. The most active isomer had the same stereochemical configuration as natural pyrethrins. J. C. Wickham (Wellcome Research Laboratories, Berkhamsted) emphasised the need for biological tests in the most realistic conditions possible in the laboratory and particular attention must be given to the size of aerosol droplets, the size of the test chamber and the adjuvant solvents in test against houseflies, mosquitoes and cockroaches; this supplemented Burt's earlier observation that there is a marked difference in effect on applying pyrethrin I in acetone to the ventral and dorsal surfaces of the housefly but no difference when the solvent is dodecane.

Moving away from pyrethroids, N. R. McFarlane (Shell Research) recorded studies on houseflies giving time and dose response curves of a closely related series of oxime carbamates. Using an analogue computer it is possible to construct models relating results to factors such as partition.

Planetary Alignments, Solar Activity and Climatic Change

JOHN GRIBBIN

Nature, 4 Little Essex Street, London WC2R 3LF

Historical data suggest a relation between the changing level of solar activity and climatic change on Earth. Since there is also evidence that the solar cycle of activity is influenced by the alignments of the planets, through tidal interactions with the Sun, it seems that climatic change might be predicted by studying these alignments.

THERE may be a causal chain linking changes in the alignments of the planets, through their tidal effect on the activity of the Sun, with climatic change on Earth. Although the separate components of this chain have been discussed before, it seems that they have not previously been linked in this way to form a coherent whole. If these ideas are correct, they provide the best basis yet found for predicting climatic changes in the immediate future.

It is convenient to assess the evidence for such a chain in the reverse direction—that is, starting from the Earth. There is good evidence that the rate at which the terrestrial length of day changes is influenced by the mean level of solar activity (see, for example, ref. 1), and although the question of a direct link between specific events on the Sun and specific changes in the length of day² seems more contentious³ it is clearly relevant to consider by what mechanism the longer term variations in solar activity affect such a gross property as the spin of the Earth. Since large scale movements of air masses associated with seasonal changes in the atmosphere are already known to produce a component in the variation of the length of day with a period of ~ 1 yr, it seems reasonable to look for the atmospheric link between changes in the activity of the Sun and changes in the spin of the Earth.

Solar Storms and Weather

In spite of the difficulty of establishing that individual large solar storms produce detectable discontinuous changes in the Earth's spin rate, there is little doubt that an increase in the level of solar cosmic rays arriving at the Earth can cause a short term change in the weather at high latitudes. Roberts and colleagues have shown (see ref. 4 and references cited therein) that troughs at high latitudes are amplified when the level of cosmic rays reaching the ionosphere (revealed, for example, by auroral activity) increases abruptly.

This discovery has obvious implications for improving short term local weather forecasting in some parts of the world. But as far as climatic changes are concerned it is

necessary to look at data averaged over at least one cycle of solar activity. King (personal communication and ref. 5) has pointed out that "it is now well established that the density and temperature of the atmosphere above about 100 km vary markedly with solar activity during . . . the 11-yr solar cycles", and he has shown that there is a positive correlation between solar radiation changes which occur during the solar cycle and meteorological variations. For example, as the level of solar activity, revealed by the number of sunspots, decreases, there is a decrease in mean temperatures and an increase in winter rainfall at Beirut. These changes seem to be related to changes in the altitude of the 500 mbar surface⁶. But even observing variations over an 11-yr period—or over several solar cycles—is not sufficient to determine patterns of climatic change.

Historical Data

Fortunately, there is a great deal of meteorological data available, and records of "good" and "bad" seasons go back for almost a thousand years⁷, in England at least. Lamb has used some of these data to determine variations of climate in the northern hemisphere and he explains them in terms of successive movements of climatic zones to south and north over periods of hundreds of years^{7,8}. According to Winstanley⁹, 1930 marked the peak of a northward excursion of climatic zones, and we are now experiencing a southward shift which has, among other effects, caused the serious drought in Africa just south of the Sahara in recent years. He foresees continued southward movement of both the Sahara and the Rajasthan Deserts until at least 2030 assuming that the present variation is part of a 200-yr cycle. The evidence for a cycle of approximately that period comes both from climatic records⁷ and from estimates of variations in the radiocarbon content of the atmosphere¹⁰; the cycle last peaked, before 1930, in the early part of the eighteenth century. It is also possible that 1930 marked the "peak" of a 700-yr cycle, although the data are not sufficient to show conclusively that such a cycle really exists.

It seems obvious to ask if there is any link between these longer term effects and the mean level of solar activity. The changes in atmospheric radiocarbon levels are particularly tantalising, since they hint at changes in the mean cosmic ray flux with period of approximately 200 yr; unfortunately, however, the only record of solar activity available which goes back for more than a few years is sunspot number, and as King points out⁵ that is a relatively crude index. Nevertheless, when sunspot numbers are plotted for this century (Fig. 1) it is immediately striking, in the present context, that the maximum number of spots, at the time of maximum solar activity, was itself a minimum in the cycle which peaked just before 1930, at the "peak" of the 200-yr climatic cycle mentioned by King. But even

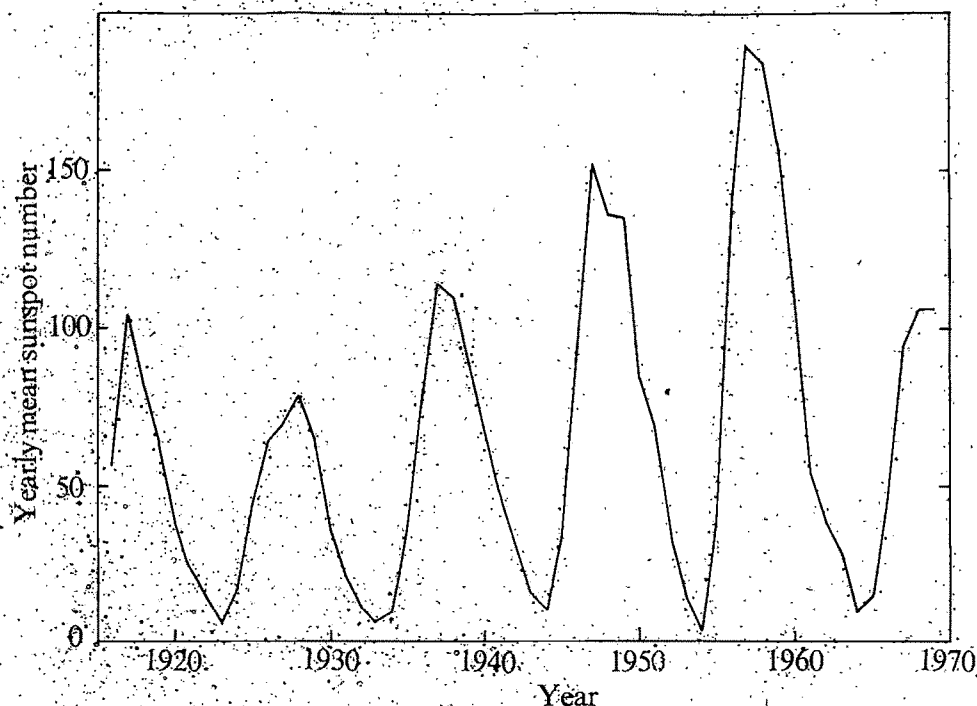
data for the numbers of sunspots at the peaks of sunspot cycles go back only to 1820—fourteen complete cycles—and there are no numerical data for cycles before 1750. Similarly, climatic data become more qualitative as one searches further into the past, and detailed quantitative data are only available for years since the mid-nineteenth century.

Possible Implications for Prediction

Attempting to establish a correlation between the two sets of data might thus seem to be foolhardy, and indeed although such attempts have been made they have met

there is a close link between the height of the tide raised on the Sun by various planetary alignments and the dates of sunspot maxima and minima; there is also a weaker link between the variation of tidal height and sunspot number¹³. That makes it possible to predict future solar activity levels, and the dates of maxima and minima, rather more accurately than simply extrapolating the average 11.1-yr cycle. And if the level of solar activity affects climate, as is strongly suggested by King's work⁵, that in turn provides a means for predicting climatic change. Perhaps the similarity between the approximately 200-yr variation of climate and atmospheric radiocarbon levels mentioned by Winstanley⁹ and the 170 to 180 (or 179?) year variation in solar activity¹³ is more than a coincidence.

Fig. 1 Yearly mean sunspot numbers during this century. (After King⁵.)



with some opposition. But the urgency of climatic research has been highlighted by recent events in Africa and India, and although it would still perhaps be foolhardy to make any conclusions drawn from comparison of these data sets the basis for immediate action, it does seem to be worthwhile to present these conclusions for discussion at the present time, when there is no completely satisfactory theory to explain climatic changes. Lamb (ref. 8, p. 443) has discussed previous attempts to relate climatic changes to long solar cycles. One of the most important of these is the discovery of a correlation between climatic series, solar variation and radiocarbon levels over more than 2,000 yr (see refs 11, 12); but in addition to the difficulty of relating past climatic changes to past changes in solar activity there is the pressing problem of predicting future climatic trends. Assuming that the correlations outlined by Lamb and discussed in detail in the references he cites do have a secure basis, is there any hope of predicting future solar activity and thus estimating future climatic effects?

Wood¹³ has noted that the maximum smoothed monthly number of sunspots for each solar cycle seems to repeat after about 170 to 180 yr. He made this discovery when analysing the available sunspot data for evidence of an influence which might be attributed to the tidal effects of the planets on the Sun; I have mentioned elsewhere¹⁴ that if this is a periodic effect then it might be linked to the 179-yr period between the alignments of the outer planets. Certainly, Wood has produced convincing evidence that

Further speculation along these lines would be inappropriate here, even granted the need for investigating all possibilities when concerned with predicting climatic change. But it does seem that climatologists and others concerned by large scale effects of changes in the atmospheric circulation such as those reported by Winstanley⁹ could do worse than to examine the predictions of solar activity made by Wood¹³ on the basis of planetary alignments.

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mRNA Transcription linked to the Morphological and Plasma Membrane Changes induced by Cyclic AMP in Tumour Cells

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Studies on a rat sarcoma link plasma membrane alterations to the activity of DNA-directed RNA polymerase II.

THE ubiquitous cell regulatory role of adenosine-3':5'-cyclic monophosphate (cyclic AMP) on a multiplicity of metabolic processes is mediated through modulation of cyclic AMP levels by intracellular adenyl cyclase and cyclic AMP-phosphodiesterase activities¹. Although the "second messenger" hypothesis² has clearly defined a major role for cyclic AMP in hormonally mediated responses, reports³⁻⁵ on the establishment of density dependent inhibition of growth in non-contact inhibited cells as well as differentiated functions⁶⁻⁸ by cyclic AMP and its dibutyl derivative suggest another major role for cyclic AMP in cell division and neoplasia. Specifically, the intracellular concentration of cyclic AMP has been implicated in the regulation of cell division *in vitro*. Rapidly growing cells exhibit relatively low levels of cyclic AMP while increasing concentrations are associated with a progressive increase in cell division times⁹. When cyclic AMP or metabolically active derivatives are incorporated in the growth media of either carcinoma⁶⁻⁸ or sarcoma³⁻⁵ cells in continuous culture, there is not only a marked growth inhibition but also a dramatic alteration in cell morphology towards that of the normal differentiated cell. Apparently related to the morphology and growth inhibition are changes in the cell surface^{10,11}. This communication links these cyclic AMP-mediated effects to the induction of mRNA by activation of nuclear DNA-directed RNA polymerase.

The *in vitro* XC rat sarcoma continuous cell line was selected as a model system for study because of its rapid growth in culture, low intracellular concentrations of cyclic AMP, and its ability to form giant syncytial cells when co-cultivated with cells producing murine leukaemia virus (MuLV)¹². Electron microscopy has revealed MuLV envelope fusion with the XC cell membrane¹³ and a heat-labile lipoprotein from MuLV has been implicated as a fusion-inducing factor¹⁴. Thus syncytial cell formation seems to be a membrane phenomenon analogous to the formation of heterokaryons by Sendai virus. We have previously demonstrated that cyclic AMP incorporated in the growth media of XC cells blocks their ability to form syncytia, decreases their agglutinability with concanavalin A, and alters their plasma membrane ultrastructure¹¹.

Using syncytium formation as an objective measure of cyclic AMP effect on membrane structure, we have demonstrated clearly, that inhibitors of transcription (actinomycin D and cordycepin) or translation (cycloheximide) block the cyclic AMP-mediated membrane phenomena in XC cells (Fig. 1). Table I summarises our experience with various cyclic nucleotides and phosphodiesterase inhibitors with respect to their ability to induce fibroblast morphology and to mediate inhibition of syncytium formation, as well as the ability of inhibitors of transcription and translation to block the effect of cyclic AMP on syncytium formation. Only cyclic AMP and its dibutyl derivative were effective. Although dibutyl cyclic AMP is effective alone, cyclic AMP requires theophylline to mediate the morphological and syncytial responses. Non-toxic concentrations of theophylline were ineffective but the more potent phosphodiesterase inhibitors, 1-methyl-3-isobutyl xanthine¹⁵ and analogues of 4-(3,4-dimethoxybenzyl)-2-imidazolidinone¹⁶ mimic the effect of cyclic AMP and dibutyl cyclic AMP, indicative of at least a partially functional adenyl cyclase. Inhibitors of transcription¹⁷ and translation block the membrane phenomena observed with both cyclic AMP and phosphodiesterase inhibitors, suggesting a common process requiring *de novo* mRNA synthesis.

Chemical probes of the mechanism of the cyclic AMP-mediated effect on transcription involved quantitation of histone and acidic (non-histone) protein content as well as activities of the nucleolar and chromatin-associated DNA-directed RNA polymerases. Figure 2 compares the histone and acidic protein with DNA ratios of a normal rat fibroblast in culture, the XC cell, and the XC cell cultivated in the presence of cyclic AMP and theophylline or theophylline alone. The histone levels are comparable in each, although the normal rat fibroblast contains more than twice the content of acidic protein than the transformed XC cell. Growth of XC cells in cyclic AMP did not alter acidic protein levels. Since the chromatin acidic proteins have been implicated in the mediation of steroid responses in certain target tissues¹⁸, as well as in the regulation of gene-expression^{19,20}, the acidic proteins of the XC cell as a function of cyclic AMP treatment were examined. SDS gel electrophoresis (Fig. 3) reveals substantial qualitative changes between the normal fibroblast and the transformed XC cell. However, cyclic AMP failed to alter the SDS pattern of the XC cell acidic proteins. Thus at this level of detection, cyclic AMP does not seem to alter the species of chromatin acidic protein present in the XC cell nucleus in spite of the obvious alterations between the normal skin fibroblast and the

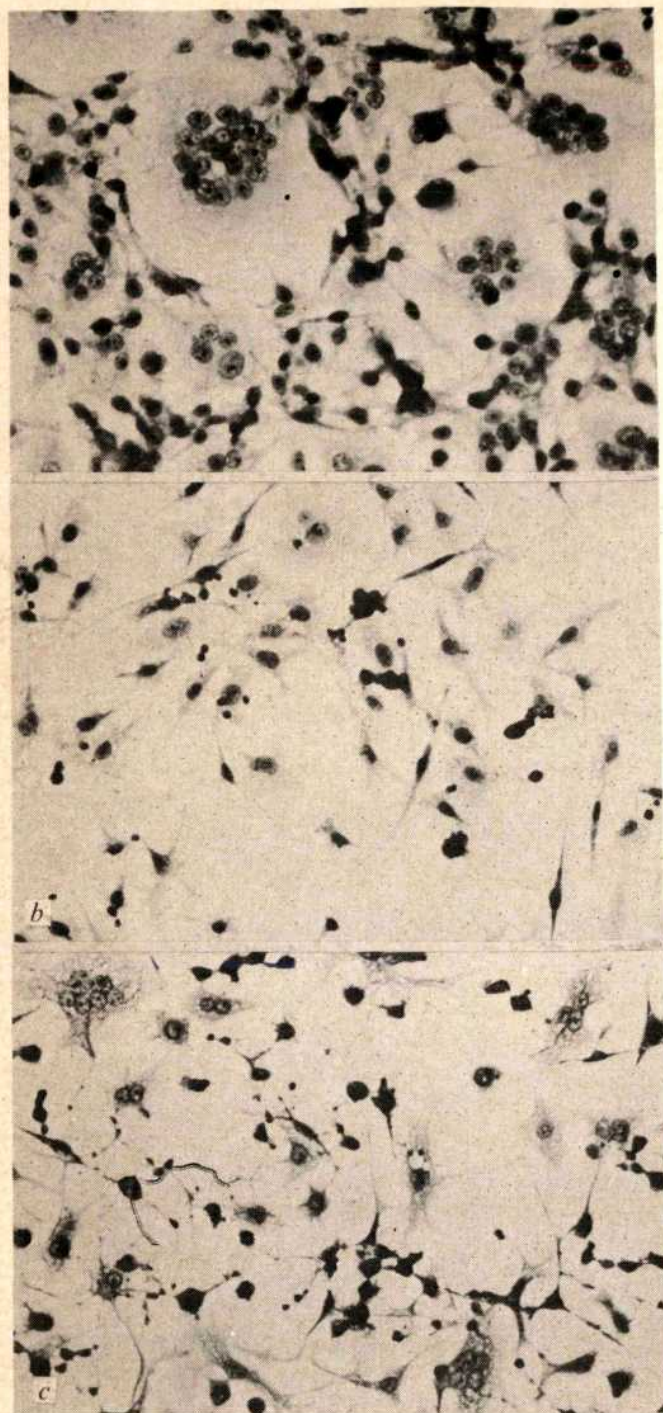


Fig. 1 Syncytial cell formation. Cells were cultivated as previously described²⁷, fixed in methanol and stained with haematoxylin. *a*, Syncytia formed after addition of MuLV producer cells (Y-1 carcinoma) (10^5 cells ml^{-1}) to rat XC sarcoma cells (10^6 cells ml^{-1}). *b*, Assay as in (*a*) except XC cells were incubated in cyclic AMP (3 mM) plus theophylline (1 mM) for 24 h before addition of MuLV producer cells. *c*, Assay as in (*b*) except that cordycepin¹⁷ ($50 \mu\text{g ml}^{-1}$) was added to the XC cell culture medium 24 h before addition of MuLV producer cells.

Endogenous nucleolar RNA polymerase activities were equivalent between normal skin fibroblasts, XC cells and the cyclic AMP-treated XC cells (Fig. 4). However, RNA polymerase II activity (DNA-like RNA transcription) was 50% that of the normal skin fibroblast. Theophylline inclusion in the growth media had no significant effect on activity but the inclusion of 3 mM cyclic AMP resulted in polymerase II

greater than the untreated XC cell. Moreover, this increase in endogenous activity accompanied a 50% reduction in the amount of open chromatin template available for *in vitro* transcription (Fig. 4). Thus the inhibition of certain cyclic AMP-induced phenomena in XC cells by inhibitors of tran-

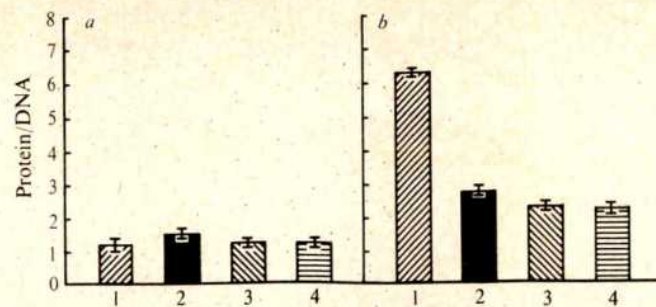


Fig. 2 Comparison of the nuclear histone (*a*) and acidic protein (*b*) composition of normal rat skin fibroblasts (derived from outgrowths of Wistar rat skin in organ culture) and XC cells. Growth medium was minimal essential medium with 10% foetal calf serum plus 3 mM cyclic AMP and 1 mM theophylline where indicated. Cells were removed by scraping and then frozen at -20°C . Nuclei were isolated at 4°C by mild cell breakage in a Teflon pestle-glass homogeniser (0.005 mm clearance) in 50 volumes (ml per ml packed cells) of 2.0 M sucrose containing 10 mM Tris, 2 mM MgCl_2 , 25 mM KCl, and 0.1% (v/v) Triton X-100 at pH 7.5 (TKM buffer), and sedimented in a Beckman 60 Ti rotor at $60,000g_{av}$ for 60 min. The nuclei were resuspended in 0.5 M sucrose-containing TKM buffer and filtered through 100 mesh organza cloth and centrifuged for 10 min at $10,000g_{av}$. These nuclear pellets were then extracted with hypo-osmotic buffer to isolate histone and nucleic-acidic protein species as previously described²⁸. 1, Normal fibroblast; 2, XC cell; 3, XC cell+cyclic AMP+theophylline; 4, XC cell+theophylline.

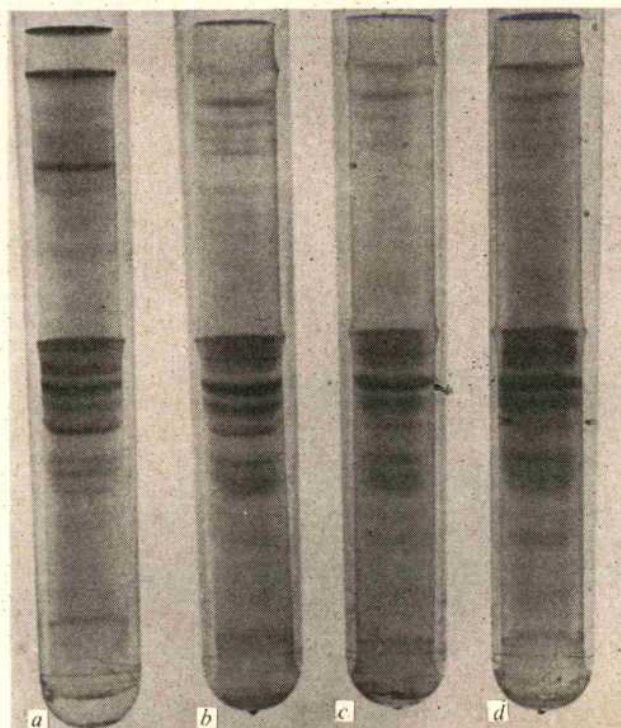


Fig. 3 SDS gel electrophoresis of the chromatin acidic proteins of normal rat skin fibroblasts and XC cells. The total chromatin acidic proteins were isolated and analysed on SDS-polyacrylamide gel electrophoresis by the method of Wilson and Spelsberg²⁹. All nuclear preparations were purified to similar degrees of cleanliness as judged by phase microscopy to avoid cytoplasmic contamination. *a*, Normal rat skin fibroblasts; *b*, XC cells; *c*, XC cells cultivated 3 d in 3 mM cyclic AMP plus 1 mM theophylline; *d*, XC cells cultivated 3 d in 1 mM

Table 1 Effect of Various Nucleotides and Phosphodiesterase Inhibitors on XC Cell Morphology, Ability to Form Syncytia, and their Blockade by Specific Antibiotics

Agent	Morphological reversion	Indicated agent only	Syncytia formation		
			Actinomycin D (5 $\mu\text{g ml}^{-1}$)	Indicated agent plus Cordycepin (50 $\mu\text{g ml}^{-1}$)	Cycloheximide (100 μM)
(A) Nucleotides					
None	—	+	+	+	+
cyclic AMP	+	—	+	+	+
dibutyryl cyclic AMP	+	—	ND	ND	ND
cyclic CMP, cyclic GMP	—	+			
cyclic UMP, or cyclic dTMP	—	+			
AMP, ADP, or ATP	—	+			
(B) Phosphodiesterase inhibitors					
Theophylline (1 mM)	—	+			
1 Me-3 iso bu xanthine (0.1 mM)	—	+			
1 Me-3 iso bu xanthine (1 mM)	+	—	+	+	+
Dime-benzyl-2-imidazolidinone (2 mM)	+	—	+	+	+
Bu, me benzyl-2-imidazolidinone (0.1 mM)	+	—	+	+	+

All nucleotides were incubated in the presence of theophylline (1 mM) at a concentration of 3 mM with the exception of dibutyryl cyclic AMP which was incubated at 0.1 mM in the absence of theophylline.
ND, not determined.

scription and translation seems to be linked to the activity of the RNA polymerase II synthesising DNA-like RNA.

Postulated Mechanism

Cultivation of XC cells in cyclic AMP or potent phosphodiesterase inhibitors results in the dramatic alteration of various morphological and biochemical processes which seem to have a common origin related to the intracellular concentration of cyclic AMP. Our evidence strongly indicates that the cell surface modifications induced by cyclic AMP and apparently shared by normal cells require *de novo* mRNA synthesis which is associated with an increase in DNA-directed RNA polymerase II activity. Although we have no direct evidence concerning the mechanism of the observed cyclic AMP-induced increase in RNA polymerase II activity, there are several possibilities. These include: (1) induced synthesis of *de novo* RNA polymerase II, (2) removal of inactivation of an

RNA polymerase II inhibitor, (3) direct activation of RNA polymerase II, or (4) indirect activation of RNA polymerase II by a secondary effector such as may occur from new synthesis; phosphorylation of sigma factor by cyclic AMP-dependent protein kinase; or conformation-induced changes in an effector. As far as we know, the only precedents concern indirect mechanisms through a secondary effector. Both phosphorylation of sigma factor of bacterial RNA polymerase by cyclic AMP-dependent protein kinase²¹ and activation of a cyclic AMP binding protein which binds to bacterial RNA polymerase²² are thought to enhance the binding of the polymerase to promoter sites on DNA²²⁻²⁴. Regardless of the mechanism of RNA polymerase activity increase, the facts that cell surface modification induced by cyclic AMP depend on mRNA transcription, are reversible and short lived^{11,25}, and are closely related to the cell cycle of the normal cell²⁶, suggest that the universal property of cell division may be regulated by the relative transcriptional activity of one or more genes continuously producing mRNA, which govern properties of the cell surface.

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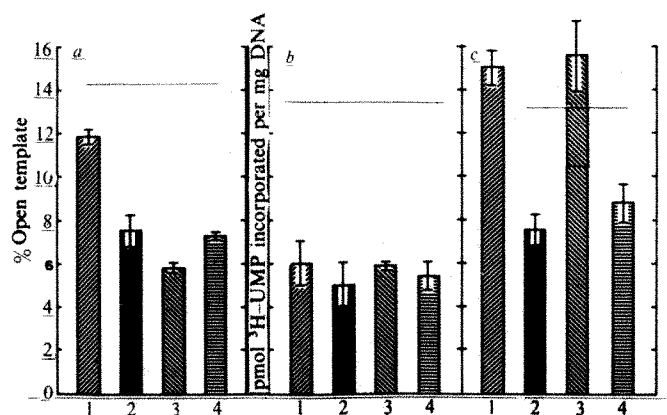


Fig. 4 Comparison of the endogenous DNA-directed RNA polymerase activities from nucleoli and nuclei as a function of chromatin template capacity. Percentage open template was assayed using *E. coli* RNA polymerase and chromatin DNA under conditions where the template is rate limiting as described elsewhere²⁹. Endogenous RNA polymerase activity was assayed as previously described^{30,31} under conditions of low salt (10 mM KCl) containing 0.2 µg α-amanitin or high salt (250 mM (NH₄)₂SO₄) which differentially distinguishes polymerase I (nucleolar) from polymerase II (chromatin-associated). *a*, Open template; *b*, nucleolar RNA polymerase (low salt); *c*, chromatin-associated polymerase (high salt). Columns are numbered as in Fig. 2.

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Origin of the West Philippine Basin

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Several alternative modes of development for the West Philippine Basin have been suggested during the past few years. The results of Deep Sea Drilling Project leg 31 indicate that none of these speculations is correct and that the basin probably formed by complex pulses of extension during the early Tertiary. A striking lineament which trends north-west across the basin, variously called the Central Basin Fault or Philippine Ridge, had previously been identified as an extinct spreading ridge of Mesozoic to early Tertiary age. On the contrary, this feature is probably a strike slip fault, possibly with a left-lateral displacement.

THE origin of the many and varied marginal basins along the rim of the western Pacific continues to provoke lively discussion.

Among these, the West Philippine Basin is the largest, and, at an average depth of nearly 6 km, approaches the depth of the mid-Mesozoic western Pacific basin. Because this great depth should imply great age¹, several recent papers²⁻⁶ have speculated that the West Philippine Basin is Mesozoic or even older, or possibly represents a section of the Pacific basin isolated by the development of ensimatic island arc systems.

We report here the results of Deep Sea Drilling Project leg 31 in the Philippine and Japan Seas (Fig. 1), as they pertain to the origin of the West Philippine Basin. These data, coupled with other unpublished information (profiles and bottom sample from Antipode cruise of Scripps Institution of Oceanography), indicate that the West Philippine Basin has not been generated as part of the Pacific basin as suggested, but is a complex early Tertiary basin developed at least in part behind a pre-existing arc system. Unfortunately, however, the possible alternative origins have only been reduced by the rejection of several possibilities. The answer remains to be gleaned from future detailed, problem-oriented studies in the region.

One speculated mode of origin which has attracted a number of recent adherents is that the West Philippine Basin was generated by crustal spreading along the Central Basin Fault (Fig. 1), either within the Pacific Basin or behind an arc system. The Central Basin Fault (profiles and bottom sample from Antipode cruise of Scripps Institution of Oceanography and refs 7 and 8) is a north-westerly trending lineament which

cuts diagonally across the basin from the Palau-Kyushu Ridge to the Palau Ridge between Luzon and Taiwan⁹. Although not explored in detail, the fault is actually a zone of very rough topography with troughs over 6.5 km deep and ridges shallower than 3.5 km. A brief local survey and available regional bathymetry suggests that the individual ridges are discontinuous and may not parallel the zone itself. At its south-eastern end, the Central Basin Fault appears to splay to a zone 300 km wide which may be curving southwards and intersecting the Palau-Kyushu Ridge at a low angle (D. E. Karig, unpublished bathymetric chart).

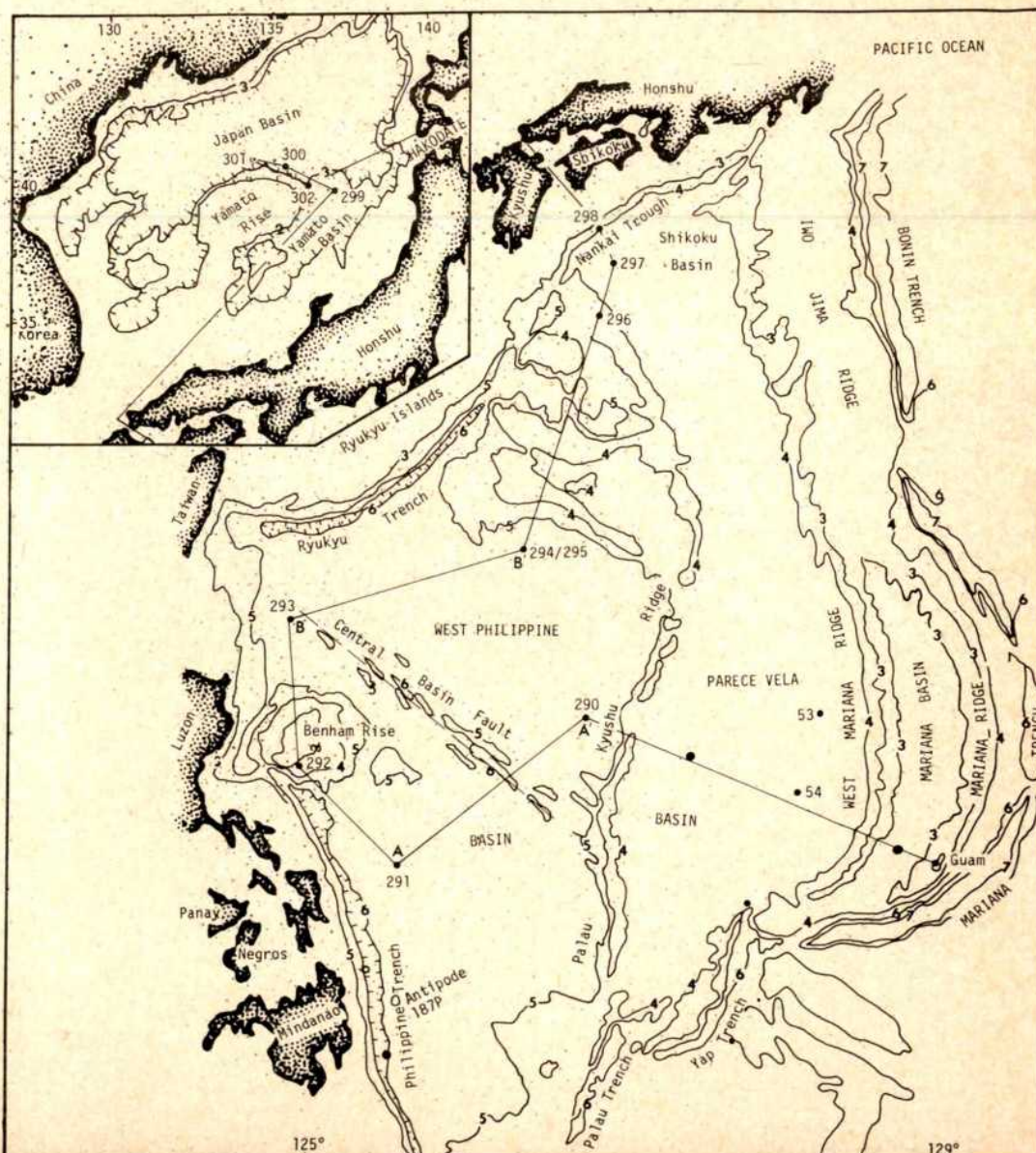
A bathymetric profile published by Ben-Avraham *et al.*³ is apparently only fortuitously similar to those across active spreading centres and is not typical of most parts of the Central Basin Fault (Fig. 2). Even in their profile, there is a discontinuity at the edge of the zone of very rough topography rather than the smooth concave upward curve characteristic of a spreading centre. Similarly, the gravity anomalies can be related simply to isostatic compensation of the larger topographic features. Their magnetic profile, which has apparent symmetry, is again not typical of other crossings of the Central Basin Fault (Fig. 2). Furthermore, brief surveys at Deep Sea Drilling Project sites 290, 291, 292, 293 and along the AT and T cable route between Guam and Manila¹⁰ show that magnetic

and topographic lineations do not parallel the Central Basin Fault, but trend NNE or less commonly NNW.

If the West Philippine Sea were Mesozoic in age and resulted from late Mesozoic spreading on the Central Basin Fault^{4,5} then the demonstrably widespread early Tertiary basalt cover must have had a very low and uniform remanent magnetism so as not to mask or disorganise the older magnetic field. The unlikelihood of such magnetic conditions, the incompatible magnetic and topographic trends, and the lack of evidence for any Mesozoic basin crust lead us to dismiss such an origin.

If, on the other hand, the crust of the basin spread from the Fault in the early Tertiary¹¹, the most plausible fit to the drilling results calls for a half rate of 2.25 ± 0.25 cm yr⁻¹ with the termination of spreading near 30 m.y. ago (Fig. 3). In this scheme, the basement of the Benham Rise would have developed after the basin formed, and reworked Eocene nannofossils found at the base of hole 293 and close to the fault would have been derived from some 300 km to the south-west from an older part of the Philippine plate which has not been subducted. At least the latter assumption is unlikely. Even so, the resulting magnetic pattern cannot be fitted to the mid-Tertiary magnetic stratigraphy and the thickness of pelagic sediment adjacent to the Central Basin Fault is too thick for a Late Oligocene age².

Fig. 1 Sketch bathymetric chart of the Philippine Sea, with track and drill sites of DSDP leg 31. Sites 53 and 54 are from DSDP leg 6; Antipode 187-P is an SIO piston core. The magnetic and bathymetric profiles on Fig. 2 are along the track between sites 290-291 and 293-294. Depths are in km.



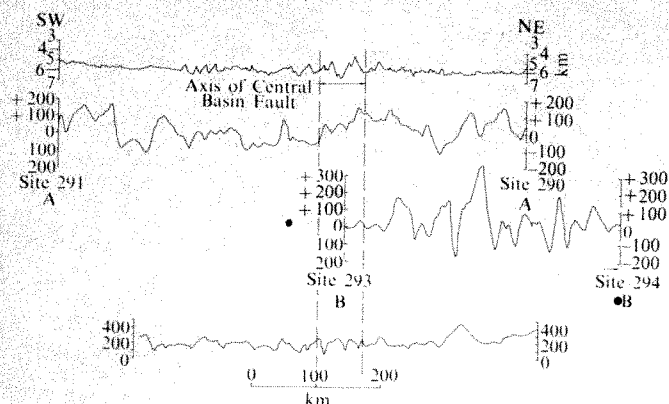


Fig. 2 Magnetic and bathymetric profiles across the Central Basin Fault in the West Philippine Basin. Profiles A-A' and B-B' are from DSDP leg 31. The lower profile is from ref. 3. All profiles have been projected normal to the Central Basin Fault, which trends 305° , and stacked so that the fault axis is represented by the vertical band. No correlation or analyses are, however, attempted.

A fit of basement ages through holes 290, 291 and 293, again assuming a younger age for the Benham Rise, would demand a pulse of spreading in early Late Eocene at a half rate of 29 cm yr^{-1} . Such spreading rates far exceed the most rapid so far postulated¹², and the corresponding Eocene magnetic pattern would have a much longer wavelength than those observed.

The lack of supporting data and the contradictory evidence presented here effectively preclude the identification of the Central Basin Fault as a spreading ridge of Tertiary or Mesozoic age. It seems more likely that, as Hess⁷ originally postulated, the fault is strike-slip in nature and probably originated as some sort of lithospheric transform. The straightness of the fault trace, the probable en echelon internal geometry, and the lack of a regional vertical displacement across the fault are the strongest lines of evidence supporting strike-slip activity.

The sense and amount of displacement are not clear, but the apparent truncation and offset of segments of the Palau-Kyushu Ridge suggest left-lateral slip of up to several hundred kilometres. Because the fault cuts the Late Eocene volcanoclastic apron drilled at site 290 and because the basement below is probably mid-Eocene, the maximum age of displacement is bounded. At the north-west end, the truncation of fault structures by a Palaeogene subduction zone⁹ and overlap by a Middle Miocene or younger sedimentary apron provide an upper limit of fault activity. The tectonic role of the fault is unknown, but it may somehow be related to the jamming of the early Tertiary west-dipping subduction zone along the eastern Luzon coast by the Benham Rise. A similar relationship has been postulated between the Ontong Java Plateau and a trench north of the Solomon Islands¹³.

Another postulated origin for the West Philippine Basin is that it represents part of the western Pacific basin trapped behind a younger arc system and modified by later volcanic activity³. This idea seems to have been engendered by the similarities in water depth and heat flow with those of the Pacific Basin and also by a faint indication of increasing thickness of the second crustal layer eastwards across the Philippine Sea. Several other observations made during Deep Sea Drilling Project leg 31 might be marshalled in support of a trapped, modified crust. The occurrence of non-calcareous brown clay lying on basalt at site 291 and possibly at site 294 suggests that the basalt was extruded below the calcium carbonate compensation depth and well after the basin crust was generated at a shallower depth. The close grouping of basement ages near Mid and Late Eocene in holes 290, 291, 292 and possibly 293 could also be interpreted as a result of widespread, flood-like eruptions.

One would, however, expect that widespread basalt flows

would either leave a few windows through which the older section could be seen, or else that the volcanic cover should be thick enough to be discerned on seismic refraction profiles. There is no place on the rather extensive reflection profile data in the West Philippine Basin where any older, uncovered section can be seen. Neither is there any evidence of a masked layer situation on seismic refraction profiles^{3,14}. To the contrary, the available data show a second layer which is as thin as or thinner than that of normal oceanic crust. There is literally no room for the insertion of a masked layer and a double basement in the crust of the West Philippine Basin.

Although the apparent re-occurrence of a Middle to Late Eocene basement age in the holes drilled in the West Philippine Basin was surprising, the total observed age spread was at least from Palaeocene (60 m.y.) to Late Eocene (40 m.y.). Volcanic activity persisting this length of time is more easily associated with crustal generation than with a pulse of subsequent volcanism.

The lack of calcareous sediments immediately above the basalt remains a puzzle. The basal calcareous brown clay of Palaeocene age at site 295 may reflect the generation of crust in the Philippine Sea when the calcium carbonate compensation depth was nearly as shallow as the crest of the spreading ridge¹¹ and beneath waters of low productivity. The relatively rapid deposition of volcanically derived brown clay at depths of 3 to 3.5 km in the Mariana Basin is presently producing such a section¹⁵, but this clay is ash-rich whereas the sections cored at sites 291 and 294/295 are not.

A variation on the trapped oceanic crust theme would have the crust of the West Philippine Sea generated along the spreading system which produced the late Mesozoic anomalies east of Japan and which has since been subducted^{12,16}. The section of the spreading ridge which lay in the area to become the West Philippine Basin has presumably been subducted or remains unidentified. This early Tertiary crust would have then been trapped behind an arc system whose age would be determined by the basal late Middle Eocene sediments on the Bonin Islands¹⁶, Siapan¹⁷, Guam¹⁸ and Palau¹⁹.

The major problem with this interpretation is that the crust in the West Philippine Basin at sites 290, 291, 292 and 293 is no older than the arcs and may even be younger. The rather mature frontal arc which reached sea level in many areas thus had very little or no time in which to develop. A suspected pre-Tertiary history of the arc systems might be read from the few Late Cretaceous planktonic foraminifera collected from the volcanoclastic apron west of the Palau-Kyushu Ridge (site 290) and supposedly derived from that ridge. Finally, there may have been as much as 45° of clockwise rotation of the Philippine

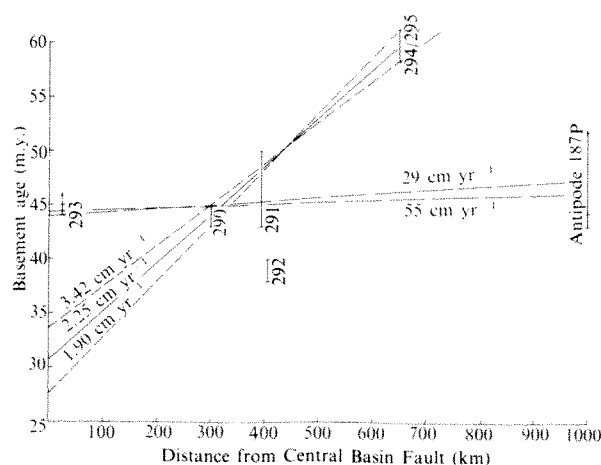


Fig. 3 Plot of basement age versus distance from the Central Basin Fault using data from DSDP leg 31 and Antipode 187-P. Shown are the range of possible half-spreading rates which could be fitted to the data. The solid bars indicate the likely range in basement age; arrows indicate minimum ages.

Plate relative to the Asian and Pacific plates during the Tertiary²⁰, but this is still a rotation insufficient to convert the east-northeast magnetic lineations east of the Japan and Bonin trenches to north-south lineations seen in the Philippine Sea.

The West Philippine Basin might instead have been produced by some form of crustal extension behind a pre-existing arc system. Within the scope of this hypothesis, extension could have occurred symmetrically, asymmetrically or in a more disorganised fashion within active marginal basins. The smaller, presently active marginal basins which have been investigated are spreading symmetrically^{9,21-23}, but if this mode continued in a basin as large as the West Philippine Basin, then a symmetrical spreading centre would no longer be located above the Benioff zone with which it is assumed to be associated.

In the West Philippine Basin the dominant north-south lineations imply an east-west spreading direction but it is difficult or impossible to choose a north-south spreading ridge which would be compatible with the known basement ages. The widespread distribution of Late Eocene basement also would require improbable rates of extension. It is therefore unlikely that a single, simple pulse of inter-arc basin extension formed the West Philippine Basin.

A new look at the West Philippine Basin suggests a more complex history, involving separate generations of subunits, some of Palaeocene or even greater age. The abundance of late Middle to Late Eocene basement in the basin and basal sediments on the surrounding arcs is indicative of a major tectonic event at that time. The northern sector of the basin seems to be older and might be related more closely to the development of the Daito-Oki Daito ridge complex which unfortunately has, so far, received very little attention.

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Molecular Model for Elastin Structure and Function

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Amino acid sequences in elastin contain striking patterns. These are interpreted in terms of possible molecular conformations, and an 'oiled coil' model is proposed to explain the protein's elastic behaviour.

THE structure-function relationships in several fibrous proteins such as collagen^{1,2}, keratin³, and silk fibroin^{4,5} are fairly clear. Elastin is an exception in spite of its role in the elasticity of

arteries, lungs, and skin, chiefly because of its lack of a good X-ray diffraction pattern^{6,7} and its extreme insolubility hindering sequence analysis. It is usually regarded as a gel of randomly coiled peptide chains, cross linked to each other^{8,9}, and attempts have been made to apply classical rubber theory to its behaviour¹⁰. Weis-Fogh and Anderson have reported^{11,12}, however, that the thermodynamics of stretching do not fit those of a normal rubber, there being strong interactions between the protein and the swelling agent (water). They therefore proposed a 'liquid drop' model, in which spherical monomers are cross linked to form a three-dimensional aggregate (compare with ref. 13). In this model, the few hydrophilic amino acids are scattered over a hydrophobic surface, and any deformation of the subunits leads to a larger hydrocarbon-water interface. This model explains very well the thermodynamics of the stretching, in which for

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a small negative free energy change (imposed stretching) there is a large evolution of heat and a high negative entropy change^{11,12}.

We have analysed amino acid sequences in a soluble elastin, isolated from aortae of copper-deficient pigs¹⁴. Several striking features of these sequences lead us to propose a new model for elastin, which, like the liquid drop model, emphasises hydrocarbon-water interactions, but views the monomeric units as fibrillar rather than globular. In our model, the principal site of hydration is the peptide chain rather than amino acid side chains. In this way, we can readily explain the high water content of elastin (50-60% by weight^{8,15}), and reversible transition to a brittle, inextensible material on drying⁷.

In spite of striking similarities in amino acid compositions, elastin and collagen seem unrelated in sequence. Hydroxyproline occurs in elastin, its principal locations being those where the local sequence resembles those that are hydroxylated in collagen (-Gly.X.Pro.Gly-):

Soluble Elastin

Mature elastin is too insoluble for extensive sequence analysis because of cross links formed from oxidised lysine residues^{16,17}. Copper-deficient animals fail to make cross links, and a soluble elastin can be isolated¹⁴. Soluble elastin from pig aorta has a chain length of 800-850 residues, based on a molecular weight of approximately 70,000 (refs 14 and 18); this is compatible with our studies of tryptic peptides^{19,20}.

Table 1 Amino Acid Composition of Soluble and Mature Elastin

		Residues per 850 residues*	
		Soluble	Mature
Gly	G	275	277
Ala	A	196	197
Pro	P	95	80
HyPro	P	7.5	12
Val	V	110	105
Ile	I	15	16
Leu	L	38	44
Tyr	Y	12	14
Phe	F	24	27
Arg	R	4.4	5.5
Lys	K	38	6
Cross links †		Very low	25-30
Asp + Asn D + N		2.7	7.5
Thr	T	12	14
Ser	S	8	11
Glu + Gln E + Q		16	18
Met + Cys + Trp + His		0	2.6

* Based on an assumed chain length of 850 residues.

† Expressed as Lys equivalents.

Modified from refs 14 and 33.

Loss of lysine and formation of cross links are the chief differences seen by amino acid analysis of soluble and mature elastins (Table 1). Notable features of the composition *per se* are: the high content of Gly, Ala, Val and Pro; the scarcity of Arg relative to Lys; absence of His, Cys, Met and Trp; and the very low frequency of polar amino acids (less than 5% total).

Amino Acid Sequences in Soluble Elastin

Sequential degradation^{20,21} of intact protein reveals one major N-terminal sequence (Table 2), plus a rather high background (10-20%).

We have previously reported the occurrence of multiple copies of the sequences -Lys.Ala.Ala.Lys- and -Lys.Ala.Ala-

Ala.Lys- in soluble elastin²² and an enrichment of Ala close to the C-terminal Lys of large (17-110 residues) tryptic peptides²³. N-terminal sequences of the latter^{20,21} are shown in Table 2.

Patterns Observed in the Sequences

Our data reveal two basic types of region in elastin: Ala- and Lys-rich areas, presumably concerned with cross linking; and Gly-, Pro-, and Val-rich areas, presumably concerned with extensibility. We do not yet know if there are many short stretches of these or a few larger ones. Within each type the observed sequence patterns suggest models for structure-function correlations.

In the cross link regions, the pairwise association of lysines and extreme enrichment in Ala are very striking. Unsequenced C-terminal portions of large tryptic peptides are enriched in Ala relative to the whole peptides; peptide T7b contains eight consecutive alanines preceding its C-terminal Lys (Table 2).

In the extensible regions, regularities occur at three levels: (1) nearest-neighbours; (2) short-range repetitions; (3) long-range repetitions. These may not be independent, as manifold repetition of a short sequence gives rise to otherwise improbable nearest-neighbour relationships, for example.

Nearest-neighbour analysis of data from Table 2 is summarised in Table 3, excluding small peptides. The principal features are: Pro is usually followed by Gly (31/36), but rarely preceded by it (4/39); large aliphatic residues are normally preceded by Gly (62/74).

Short-range repetitions of sequence are a most notable feature of the data (underlined in Table 2). The limited divergence within peptides T1, T2 and T7a suggests that some of the local duplications are recent. In other peptides there are suggestions of regularity, more or less obscured by amino acid substitutions and deletions. The elastin gene could be considered as a microcosm of the whole DNA, containing families of repeated sequences varying in ages and degrees of relation²⁴. Multiplication of short sequences could be a powerful force in the evolution of structural proteins because of the speed with which radically new properties can appear. Silk fibroin sequences such as (-Ser.Gly.Ala.Gly.Ala.Gly-)_n are closely related to elastin sequences such as (-Pro.Gly.Val.Gly.Val.Ala-)_n. A few point mutations, plus genetic amplification, can lead from one structure to the other.

Long-range repetitions are suggested by marked similarities between different peptides, but cannot be defined accurately until more is known of the order of peptides in the molecules. A plausible mode of evolution of elastin involves duplication of large segments each containing a cross link site and some extensible region. Present evidence suggests there may have been a six- or eight-fold multiplication.

Molecular Models for Elastin

The regularities of primary structure prompted us to examine possible regular structures for elastin. For this we used CPK atomic models²⁵ and conformational maps²⁶ to help avoid too-close contacts. The cross link regions will be discussed only briefly as a full discussion is in preparation (W. R. G., L. B. S. and J. A. F., manuscript in preparation).

In the cross-link regions, pairs of lysines occur in sequences such as -Ala.Ala.Ala.Ala.Lys.Ala.Ala.Lys.Tyr.Gly.Ala.Ala-; the sequences could be much longer, with more lysines and with longer runs of alanine at the amino end. Such regions would favour an α -helical conformation, with lysines protruding from the same side of the helix; this facilitates intrachain condensations between oxidised lysines. Subsequent interchain condensations lead to desmosine and isodesmosine linking two α -helical chains, with very little strain. Estimates of helical content of hydrated elastin vary from 10-25%, depending on the model system used and on correction factors^{27,28}. Cross-link areas might be expected to contribute 15-20% α -helix.

Table 2 Amino Acid Sequences in Soluble Elastin

Large tryptic peptides*		1	5	10	15	20	25	30	35	40	45
T 15 (88 residues)		G G V P G A V P									
Whole protein		G G V P ₁ G A V P ₂ G G V P ₃ G G V F ₄ F P G A G L G G L G									
T 1 (85 residues)	(K)	Y G A A G G L V P G A P G F G P G V G V ₁ P G V G V ₂ P G V G V ₃ V ₄ P G V g V ₅ P G V g v									
T 4 (110 residues)	(K)	Y G A P G A G V L P G V G V G G V g v p g									
T 9c (30 residues)	(K)	Y G A A G A L G G V G B L G G A G I P g x v A G									
T 2 (60 residues)		A A Q F G L G P G I G V A ₁ P G V G V A ₂ P G V g v A ₃ P G V G V a ₄ P G V G V A ₅ P x I ₆									
T 9b (36 residues)		A A E F G V G G V G G L x v G G L G A V x G A G									
T 6 (40 residues)		A G A G L G G V G G V G G L G V s T G A V V P									
T 14b (39 residues)		A P G G G G A F A G I P G V G G ₁ F G G Z Z P G V P L x G p									
T 7a (58 residues)	(R)	G G V G V G G I P T F G V G A G G F ₁ G F G V G V G G V p G A A L									
T 12 (24 residues)		V P G V G L ₁ G V Y P G									
T 14c (17 residues)	(R)	F P G V G V L P G V P T G T G V K									
T 7b (21 residues)		A G Y P T G T G V G T Z A A A A a A A A K									
Small tryptic peptides† (Mol per mol protein)		C-terminal fragments of large tryptic peptides‡									
A A A K (6)		A P G K (2)								A K (7.3)	G K (0.5)
A A K (6)		A K (1)								A A K (4.5)	G V K (1.2)
S A K (2)*		Y G A R (2)								A A A K (0.9)	G P K (0.5)
										G A K (0.8)	G A R (1.3)

Abbreviations as in Table 1; B, Asp or Asn; Z, Glu or Gln; x, unknown; lower case letters indicate residues that are identified with a lower degree of confidence. Only the principal hydroxylation sites are indicated as P.

* Ref. 20, plus some previously unpublished data. All except T14c and T7b are partial sequences.

† Ref. 22.

‡ Ref. 23. Results are expressed as mole per mol protein, based on assumption that all fragments were recovered in equivalent yield. (Measured overall yield was 70%.) The method used underestimates presence of sequences such as A A K, since some appears as A K and A K.

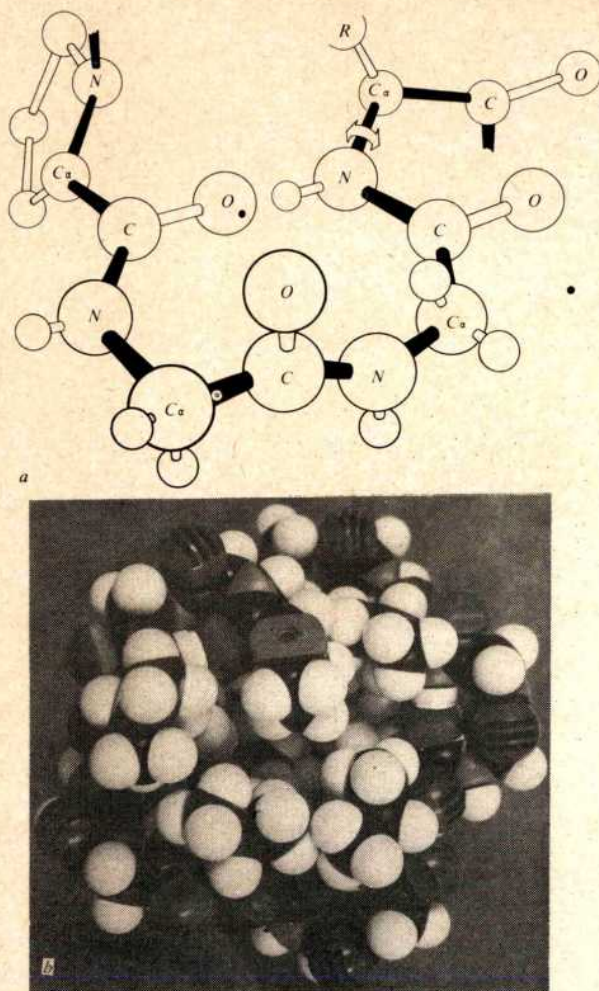


Fig. 1

Regions between cross links are depleted in Ala and rich in Gly, Pro, and Val; these presumably control the protein's extensibility. Two extreme views can be held about the chains here. In one, the chain is randomly coiled and kinetically free, as in 'classical' rubbers^{8-13,15}; in the other, the chain has a preferred conformation that is returned to after release of a stretching force. Probably a dynamic blending of the two is most realistic.

Measurements of heat changes during reversible stretching

Table 3 Nearest-neighbour Relationships in Elastin

First residue	Second residue				
	Gly	Ala	Pro	Val + Leu + Ile	Others
Gly	22	16	4	62	9
Ala	12	12	8	5	4
Pro	31	0	0	1	4
Val + Leu + Ile	36	6	21	4	5
Others	14	2	6	2	7

Compiled from data of Table 2, excluding the small peptides and fragments.

suggest strongly that hydrophobic groups are forced into water during stretching and that energy for contraction comes from the return of these groups to a non-polar environment^{11,12}. We propose that these interactions are controlled by definite conformations of the protein, and that the observed sequence patterns reflect the constraints imposed by the secondary structure.

We have discovered some plausible structures for the amino-terminal type of repeat that immediately suggest a working model for the extensibility of elastins. Other repeat sequences can assume conformations having the same general properties. The main feature of our model is a broad coil in which glycines occupy the exterior positions exposed to solvent, while Pro, Val, and other hydrophobic residues are buried; most of the peptide backbone is hydrated. For descriptive purposes we call this general type of structure an 'oiled coil'.

A β -turn^{29,30} made from the tetrapeptide -Pro-Gly-Gly-Val- is shown in Fig. 1a. It forms a compact block with the bulky hydrophobic groups at one end and the glycines at the other. When several such blocks are linked, they make a broad left-handed helix (Fig. 1b) with bulky side chains in the centre and glycines on the outside; this creates a natural inside and outside in aqueous conditions, the exposed peptide chain being hydrated. No H-bonding occurs along the direction of the helix axis, so the coil is readily extended by rotation around the C_{α} -CO bond of Pro (decrease Ψ) and around the Val C_{α} (decrease ϕ , increase Ψ). A 30° decrease in Ψ for Pro, with appropriate changes for Val, produces an extension of about 2.5 Å for every tetrapeptide unit in the coil, more than doubling the length of such regions. Although extension does not disrupt intrachain H-bonds, it is energetically unfavourable on two counts. First, it exposes the hydrocarbon core of the coil to water, leading to structuring of the water and an unfavourable entropy decrease; this fits the observed thermodynamics of stretching^{11,12}. Second, the conformation of Val becomes less favourable, judged by conformational maps²⁶. Release of the stretching force should thus lead to contraction to the original state.

Beta-turns themselves are not very restrictive, and suitable conformations can be found for almost any group of amino acids³⁰. To produce an oiled coil structure from them, however, puts limitations on the polarity of the various residues. For the structure described, maximum stability requires hydrophobic groups in positions 1 and 4 and polar groups in positions 2 and 3.

Urry³¹ discussed β -turns as binding sites for calcium in elastin, using peptide antibiotics as models. We feel that conformations with bound calcium are likely to be inside-out with respect to hydrophobicity; this is acceptable for molecules functioning in a non-polar environment such as a cell membrane but not for a hydrated elastin fibre. Binding of calcium would stabilise a rigid inside-out conformation.

Repeating sequences such as (-Pro-Gly-Val-Gly-Val-Ala-)_n and (-Pro-Gly-Val-Gly-Val-)_n were found after we had developed the oiled coil model for the tetrapeptide. So far we have not found β -turn structures for these that have such a clear inside-outside character, but structures other than the β -turn can give rise to the same properties (Fig. 1). In such structures the role of Gly may be as much steric as hydrophilic since it alone allows the chain to fold back so tightly.

Overall View of Elastin Model

Our model for elastin is outlined in Fig. 2. Each monomer is fibrillar, and made up of alternating segments of cross link regions and 'oiled coils'. The mechanical properties of these are quite distinct, being rigid and flexible, respectively. Each monomer is linked to many others, forming a network like a three-dimensional mattress spring. Chains may be cross linked at various angles, or bent, so the networks could be isotropic, despite the fibrillar nature of the monomers.

Our scheme for the process of cross linking makes predictions about the mechanical properties of elastin. Thus 'cross links' formed from two lysine residues are local intrachain knots and not true cross links, and each residue of desmosine and isodesmosine cross links only two chains, rather than the three or four which it is potentially able to. From the known cross link content of mature elastin, therefore, the average chain mass between cross links (M_c) would be about 7,000 daltons; other cross linking schemes give M_c as low as 2,000–4,000 daltons.

The diameter of the 'oiled coils' is about 12–15 Å and the hydrophobic core can accommodate non-polar molecules, especially straight-chain aliphatic compounds. Partridge^{8,9,13} investigated the gel-filtration behaviour of a number of compounds on columns packed with elastin fibres. He found that elastin could be regarded as being made up of randomly disposed hydrated rods about 16 Å in diameter, with free water spaces between them. Aliphatic alcohols showed anomalous behaviour, partitioning preferentially within the gel particles, the effect being greater for *n*-alcohols than for branched. We suggest that they might be fitting within the core of the coils, rather than adsorbing on to the surfaces.

From the composition, we estimate that 20–25% of the molecule should be in cross link regions, with the rest as coil—the two forms then contribute equally to the length of the relaxed monomer. Extension of the coils proceeds smoothly until the whole molecule is 2–2.5 times the original length. Stretching increasingly exposes the hydrocarbon core to water; this should lead to restructuring of the water, accompanied by the thermodynamic changes observed by Weis-Fogh and Anderson^{11,12}.

M_c varies inversely with the elastic modulus of the rubber if it can be assumed that the contractile force is generated solely by entropic diffusion of the macromolecular chains. The stress-strain behaviour of elastin has been measured in various solvents, enabling M_c' to be estimated¹⁵. (We use M_c' to indicate values of M_c measured from stress-strain behaviour on the assumption of random kinetic diffusion of chains. M_c denotes actual mass of chain between cross links.) In aqueous formamide (40% v/v), M_c' reaches its maximum of about 7,200 daltons, close to our predicted value. In these conditions, we expect the protein chains to be completely unfolded so that elastin should behave as an 'ideal rubber' with M_c' representing the true mass between cross links. In water, M_c is 3,500 daltons, corresponding to an increased elastic

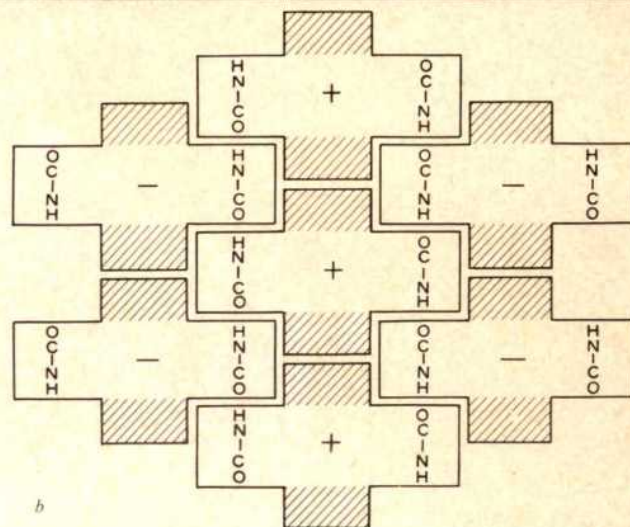
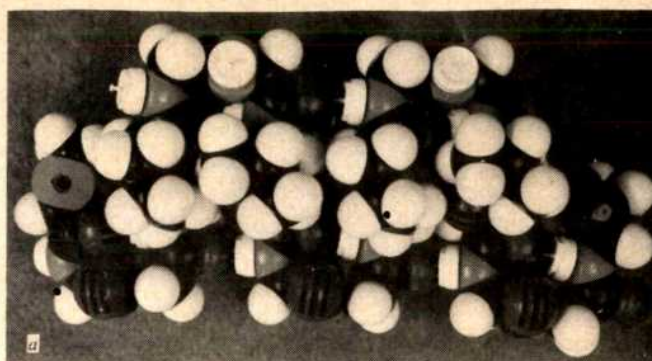
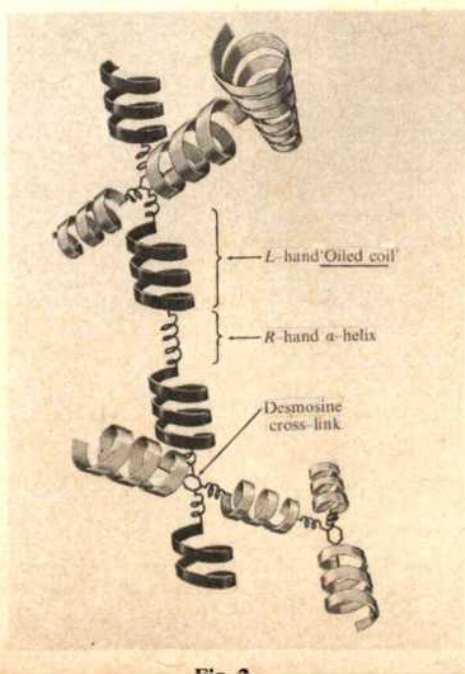


Fig. 3



modulus. We interpret this as being due to two main causes. First, lengths of chain in the cross link areas are rigidly attached to the cross links and not free to diffuse; second, the oiled coils generate an additional contractile force due to the interaction of their hydrophobic groups with water. In conditions likely to disrupt hydrophobic interactions but leave α -helix unaffected (for example, 8% v/v aqueous butanol), M_c' is about 5,400 daltons, which corresponds with our estimate of the average mass of the coil regions. These conditions also cause profound changes in the thermodynamic parameters of elastin stretching^{11,12}.

When dried, elastin becomes brittle, its elastic modulus being three orders of magnitude greater⁷ than that of the hydrated form (50–60% water by weight). Such a transition, which is reversible, is remarkably easy to accomplish with our model for the oiled coil form of $-(\text{Pro.Gly.Gly.Val})_n-$. When the Val N-C α bond is rotated by about 180°, the tetrapeptide units stack quite differently, forming a modified cross- β structure (Fig. 3). The repeat distance is four residues, with two H-bonds between neighbouring antiparallel segments of chain (proline residues prevent formation of a third). Peptide bonds in the β -turns are perpendicular to the chain axis so systematic H-bonds form between chains of opposite polarity. Hydrophobic side chains form two ridges that interact between chains of the same polarity (see Fig. 3). Similar cross- β structures can be made from the hexapeptide and pentapeptide, the latter having a repeat period of ten residues. Such a structure, cross-linked by H-bonds, would have a much higher elastic modulus than the oiled coil; transition from high to low modulus occurs close to the point (30% water by weight) where there is one water molecule for each peptide carbonyl and amide group.

Our general model for elastin thus provides a molecular basis for the behaviour of the protein, and clarifies several features that are not readily explained by a model that invokes

only the usual entropic diffusion of randomly coiled chains. It does, however, suggest a static molecule in which chains are coiled in a particular way, and return to the same conformation each time after stretching. Recent ^{13}C -NMR studies, on the other hand, indicate high mobility of the peptide chain in native elastin³². We suggest that this is caused by oscillation and flexion of the network of coils, rather than by completely random segmental motion of its microscopic parts.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Radio Detection of Interstellar CH

As recently as 1968 the only molecules known to exist in interstellar space were CH, CH⁺ and CN, identified by means of their absorption spectra superimposed on the optical spectra of bright stars, and OH which in its ground state emits at a radio wavelength of 18 cm. Since then there has been a remarkable series of discoveries of about twenty additional molecules emitting in the radio spectrum, some of them quite complex (CH₃OH for example). But of the originally discovered 'optical' radicals, only CN, emitting at about 2.6 mm, has been detected at radio frequencies—in the Orion Nebula, in the HII region W51, and in the infrared object IRC+10216. The other radical, CH, has not been found, mainly because the radio frequencies of its ground state lambda doublet have not been found in the laboratory, and it has not been possible to compute them theoretically with sufficient accuracy. The first estimate of the (main line) frequency seems to have been made by Shklovsky¹: $3,180 \pm 10$ MHz.

Two previous searches for CH with the 84-foot radio telescope of the Onsala Space Observatory (Rydbeck and Elldér), in September 1968, covering the range 3,000–3,135 MHz, and in October–November 1971, covering 3,361–3,385 MHz, proved negative².

We resumed the search in October 1973 with an improved rutile travelling wave maser and linear polarisation (zenith system noise 35 K), and have now succeeded in detecting the ground state lambda doublet ($^2\Pi_{1/2}$, $J=1/2$) at a wavelength of approximately 9 cm in the direction of the following objects: W3OH, W3 Cont, W12, Orion A, W31, W43N, W44, W49,

W51, DR21, W75 B, Heiles clouds 2 and 1B, Cudaback–Heiles cloud G84.7–1.0, Lynds cloud L134, and Cas A (Orion and Perseus arms). Since the transition was seen in HI and HII regions, as well as dust clouds, there is reason to believe that CH is widespread in our Galaxy.

CH was seen in emission in all objects, and not in absorption even in Cas A, W12, and cloud G 84.7–1.0, as one might have expected from OH observations. This is especially remarkable in the direction of Cas A, where CH seems to behave like a weak maser. One can only guess about the possible mechanism of inversion of CH in the 'clouds' in the direction of Cas A. Reactions leading to the formation of CH might leave it in an inverted ground state. Collisions with hydrogen atoms could perhaps have the same effect. In the cool dust clouds, on the other hand, where molecular hydrogen is prevalent, such a collisional effect seems less likely.

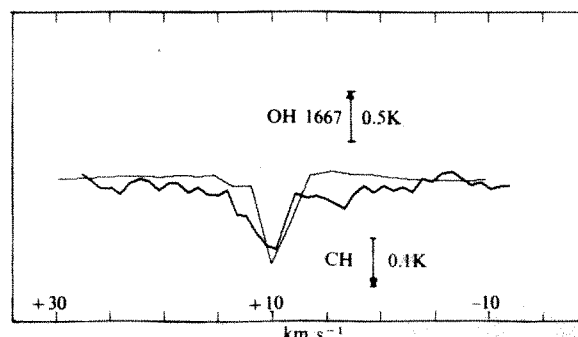


Fig. 1 W12, CH (—) and OH 1667 (RC+LC)/2 (---)

We have not seen CH in the anomalous, strong emission which is frequently observed for OH in HII regions. Nor was there any evidence of magnetic splitting. In this respect CH seems to resemble OH in its excited $^2\Pi_{1/2}$, $J=1/2$ state.

The CH features are very well correlated with OH main line absorption and thermal emission features. The correlation with the formaldehyde spectra is also quite good. The rest frequency of CH, as determined from comparison with 1,667 OH features in W12, Heiles cloud 2, Lynds cloud L134, and Cas A, is $3,335.475 \pm 0.010$ MHz. The error corresponds to the width of the channels, 10 kHz, of the multi-channel post amplifier used. We expect to improve this somewhat by the use of our 1 kHz filterbank system. It is interesting to compare this frequency with the values predicted by Goss³ in 1966, $3,030 \pm 38$ MHz, and by Baird and Bredohl⁴ in 1971, $3,374 \pm 20$ MHz.

We have looked for CH in one strong OH infrared object, NML Cyg. There is evidence of a faint emission, but our results are not conclusive at this point. Should the results ultimately prove to be negative, one is tempted to believe that CH is very faint or absent in objects which seem to lack formaldehyde. Thus it is not surprising that CH is quite weak in Orion A, which is known also to be weak in formaldehyde.

To illustrate the discussion we have depicted in Figs 1 to 7 the new CH spectra together with OH and H_2CO spectra obtained with the Onsala rutile travelling wave maser radiometers^{5,6} in the following typical sources: W12, Lynds cloud L134, Heiles cloud 2, Cas A, W43N, DR21, and W51. In the figures RC and LC denote OH spectra determined with right and left hand circular polarisation filters, respectively. The OH and H_2CO spectra have been plotted at a resolution of 10 kHz to facilitate comparison with the CH profiles. Note that the direction of positive antenna temperature, as indicated by the arrows, is opposite for CH compared to OH and H_2CO .

The pertinent data from all our observations, excluding NML Cyg, are summarised in Table 1.

We acknowledge help from Dr E. Kollberg and Mr C.-O.

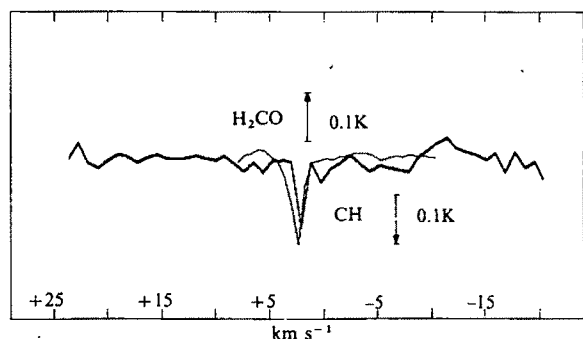


Fig. 2 Lynds cloud L134, CH (—) and H_2CO (—) ground state spectra.

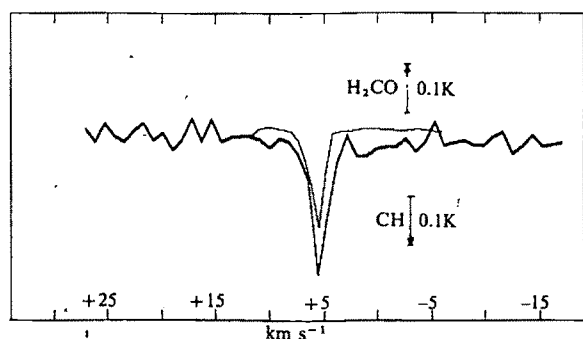


Fig. 3 Heiles cloud 2, CH (—) and H_2CO (—) ground state spectra.

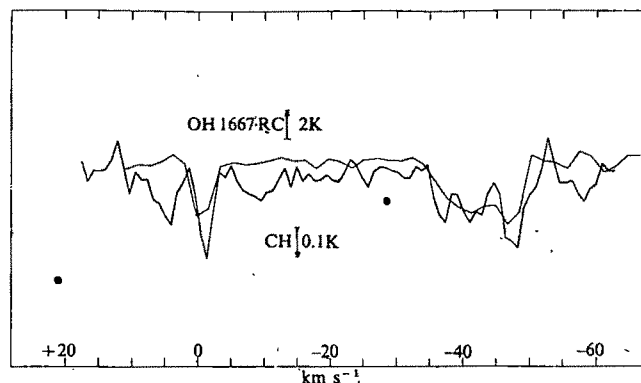


Fig. 4 Cas A, CH (—) and OH 1667 RC (—) spectra.

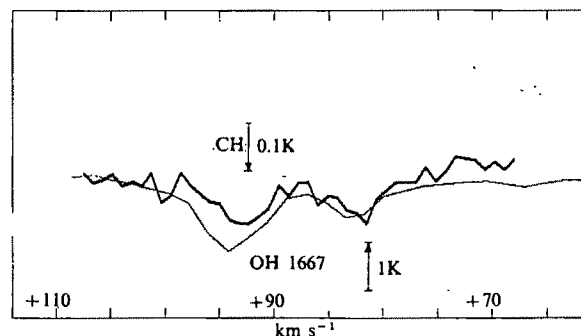


Fig. 5 W43N, CH (—) and OH 1667 (RC+LC)/2 (—) spectra.

Lindström of the Quantum Electronics Group, Research Laboratory of Electronics, and discussions with Drs T. Cato, Å. Hjalmarson, B. Höglund, and Mr A. Sume, who assisted with many of the reductions. We also thank Messrs C. Andersson, S. Hansen and J.-Å. Gustafsson for help with the observations. This research was partly supported by the Swedish Natural Science Research Council and the Swedish Board for Technical Development. One of us (W. M. I.) acknowledges support under the programme of Senior Scholar Exchanges between the United States and the USSR.

Note added November 19. After these observations were concluded, we also succeeded in detecting both the upper and the lower satellite lines of the ground state A doublet of CH. Their frequencies have been found to be $3,349.185 \pm 0.010$ MHz and $3,263.788 \pm 0.010$ MHz. Like the main lines the satellite lines have so far been seen in emission only, even in the direction of the radio source Cas A—a notable circumstance. Although

Table 1 Properties of CH Emission (Onsala Space Observatory)

Object	α_{1950} (h min s)	δ_{1950} (° ' ")	CH velocity of max. feature (km s ⁻¹)	CH, approx. antenna temp. (K)
W3OH	02 23 17	61 39 00	-47	0.05
W3 Cont	02 21 55	61 52 00	-40	0.07
W12	05 39 12	-01 57 42	+9.5	0.15
Orion A	05 32 47	-05 24 21	+10	0.08
W31	18 07 34	-19 56 30	-1.5	0.04
W43N	18 45 01	-02 00 03	+92.5	0.09
W44	18 50 48	01 11 07	+56	0.12
W49	19 07 53	09 01 00	+15.5	0.07
W51	19 21 27	14 24 30	+65	0.10
DR21	20 37 14	42 09 00	-2.5	0.12
W75 B	20 36 50	42 26 58	-2.5	0.06
Heiles 2	04 38 30	25 38 00	+5.5	0.28
Heiles 1B	22 27 55	74 58 00	-4.5	0.08
G84.7-1.0	20 54 23	43 30 00	+0.5	0.15
Lynds				
L134	15 50 54	-04 31 00	+2	0.15
Cas A	23 21 11	58 32 48	-1/-48	0.28/0.24

the intensity of the upper satellite line is roughly 50% of that of the main line (the local thermodynamic equilibrium ratio), the corresponding ratio of the lower satellite to the main line seems to differ from this value in some cases. We classify the transitions as follows:

$$\nu_{10}(F=1 \rightarrow 0+) = 3,349.185 \pm 0.010 \text{ MHz (the upper satellite line),}$$

$$\nu_{11}(F=1 \rightarrow 1+) = 3,335.475 \pm 0.010 \text{ MHz (the main line, } \Delta F=0)$$

and

$$\nu_{01}(F=0 \rightarrow 1+) = 3,263.788 \pm 0.010 \text{ MHz (the lower satellite line).}$$

The ground state $^2\Pi_{1/2}$ $J=1/2$, Λ doublet of CH is a triplet since the ν_{00} -transition is 'forbidden'. In this context it should be mentioned that the four lines of the $^2\Pi_{1/2}$, $J=1/2$ ground state OD Λ -doublet lie in the range 3,090 to 3,115 MHz, that is, well below the CH frequencies.

It is interesting to compare the magnetic hyperfine splittings of the $^2\Pi_{1/2}$, $J=1/2$ state of CH with those of OH, as shown in Table 2. Since none of the CH lines have so far been seen in absorption, irrespective of the nature of the source where they have been found, one is led to believe that all transitions are masing weakly. It could, therefore, very well be that ground state CH is formed totally inverted. This might have important consequences for our understanding of the CH chemical reactions and their rates in the interstellar medium.

Table 2 Comparison of Hyperfine Splittings

Hyperfine splitting	CH	OH
-Parity level (MHz)	71.687	90.414
+Parity level (MHz)	13.710	14.906

Figure 8 shows, as a typical example, the good correspondence between the ν_{10} , ν_{11} and ν_{01} spectra as seen in the direction of W12. The upper satellite and the main line are quite similar in shape. The lower satellite spectrum, on the other

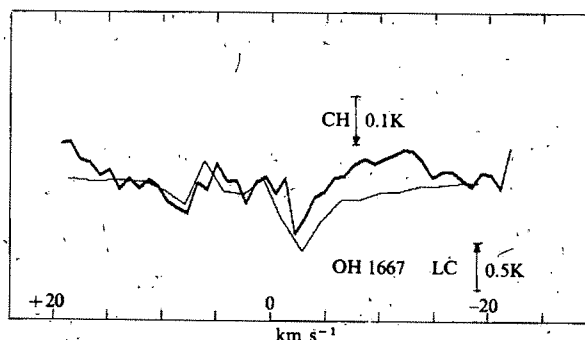


Fig. 6 DR 21, CH (—) and OH 1667 LC (---) spectra.

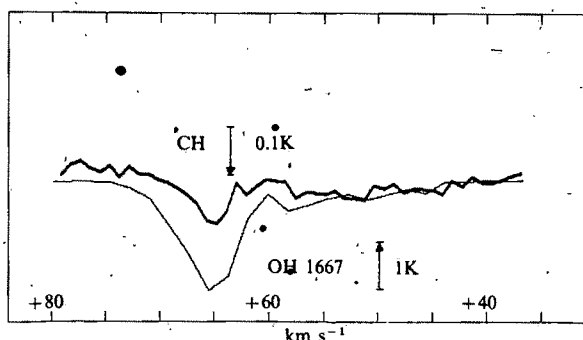


Fig. 7 W51, CH (—) and OH 1667 (RC+LC)/2 (---) spectra.

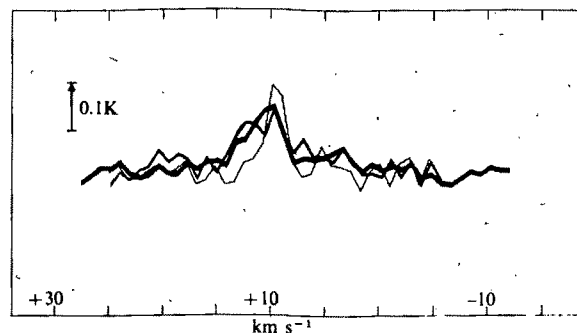


Fig. 8 Emission spectra of the ν_{11} (heavy line), ν_{10} (medium), and ν_{01} (light) lines of the CH ground state Λ doublet, as seen in the direction of W12.

hand, is narrower and has a larger amplitude. Evidently the latter is more strongly masing than the other lines. The same phenomenon is also apparent in the -48 km s^{-1} feature in the direction of Cas A, whereas the ratios between each of the satellite lines and the main line are approximately equal to 0.5 in G84.7-1.0 and Heiles 2. Longer integration times are needed to determine these ratios, as well as the rest frequencies, more accurately. Details of the interstellar satellite line spectra of CH will appear in ref. 7.

We thank Mr Christer Andersson who took an active part in the rapid discovery of the satellite lines, and especially Dr T. Cato who assisted us in the computation of the hyperfine splitting of the ground state doublet.

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TiO₂ and a Possible Guide to Past Oceanic Spreading Rates

THE work reported here shows that there is some sort of systematic relationship between the titanium content of present-day ocean-floor basalts and spreading rate. This simple geochemical indicator can be applied to estimate ancient spreading rates using basalts and spilites from ophiolite complexes.

Titanium, expressed as TiO₂, was chosen because it satisfied the following conditions: a reasonable quantity of available data; a good degree of variation between fast and slow spreading ridges; stability under conditions of weathering and zeolite or greenschist facies metamorphism encountered in altered lavas from most ophiolite complexes¹. The data were selected from published major² and trace^{3,4} element analyses of ocean-floor basalts. Picritic lavas containing cumulus crystals of olivine were eliminated as were the rare silicic differentiates and rocks collected from or near to

oceanic islands. Samples from locations that were not known with sufficient accuracy for the spreading rate to be determined were also ignored. Samples from the equatorial Atlantic, for instance, were rejected because they may have been generated at 'leaky' transform faults. In all, 171 TiO_2 analyses were used, representing almost all suitable analyses so far published.

Error in spreading rates is difficult to determine. Most rates are averages over the time interval of magnetic anomalies (several million years) whereas basalt compositions may reflect the rates during the times the magmas they represent were generated. The most recent published sources of rates were used here⁵⁻⁷. The location, spreading rate and mean TiO_2 contents for the samples are listed in Table 1. Also in Table 1 are the standard deviations about each mean which give some idea of the spread of values at each locality. The means and standard deviations were both calculated on the assumption of log-normal distribution which has been shown to be most appropriate to this kind of system⁸.

Figure 1 shows the result of plotting mean TiO_2 values against spreading rate on logarithmic axes. A linear regression line and a correlation coefficient were calculated from points based on more than a single sample. The correlation coefficient of 0.7784 for twelve degrees of freedom is significant at around the 0.001 level. Samples from location C5 have been altered and their spreading rate is uncertain. If this location is omitted, a very similar line is obtained, with a correlation coefficient over 0.8. The level of significance suggests that this logarithmic relationship between TiO_2 and spreading rate is real and not due to chance.

Table 1 Summary of Data Used to Relate TiO_2 and Spreading Half Rate

Location	No. of analyses	Spreading half rate	Mean TiO_2	Standard deviation bars (± 1 s.d.) for mean TiO_2
A1 Atlantic 65°–50° N ⁵	13	1.2	1.06	0.99–1.14
A2 Atlantic 50°–35° N ⁵	20	1.3	1.34	1.19–1.52
A3 Atlantic 35°–20° N ⁵	51	1.5	1.51	1.32–1.72
A4 Atlantic 20°–5° N ⁵	1	1.6	1.46	—
A5 Atlantic 41° N 14° W ⁵	4	2.5	1.61	1.19–2.17
PR Palmer Ridge ⁵	8	1.0	1.07	0.90–1.27
JF Juan de Fuca Ridge ⁷	9	2.9	1.78	1.50–2.11
E1 East Pacific Rise ⁷	2	6.7	1.74	1.22–2.49
E2 East Pacific Ridge ⁷	1	8.2	2.10	—
AF Alula-Fartak Trench ⁶	23	1.0	1.41	1.22–1.63
GA Gulf of Aden ⁶	7	1.0	1.02	0.88–1.17
C1 Carlsberg Ridge ⁶	8	1.3	1.46	1.32–1.61
C2 Carlsberg Ridge ⁶	3	1.4	1.42	1.24–1.63
C3 Carlsberg Ridge ⁶	4	2.3	1.38	1.30–1.47
C4 C Indian Ocean Ridge ⁶	10	3.0	1.42	1.24–1.64
C5 C Indian Ocean Ridge (non-axial) ⁶	7	6.5	1.91	1.80–2.02

The means and standard deviations for TiO_2 were calculated on the basis of log-normal distribution.

The explanation of the correlation presumably lies in the variables usually used to explain trace element contents of magmas: depth of melting and liquid segregation, mineralogy and chemical composition of the mantle, degree of partial melting, wall-rock reaction, and crystal fractionation on ascent to the surface. At this stage more information seems to be needed in order to decide how these variables differ in fast and in slow spreading ridges.

Application of the results to basalts and spilites from Phanerozoic ophiolite complexes first requires proof that the lavas in question were erupted at mid-ocean ridges and not in volcanic arc, continental or ocean island situations. Methods have been proposed to do this using Ti, Zr, Y and Sr^{3,4,9} and rare earths^{10,11}. We have chosen the lower pillow lavas of the Troodos Massif of Cyprus as an example of an

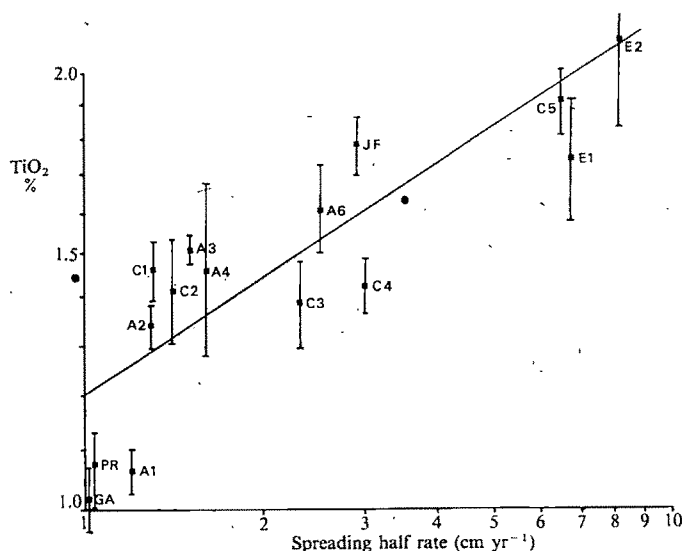


Fig. 1 Logarithmic plot of mean TiO_2 against spreading half rate for the localities in Table 1. The bars show the standard errors ($\sigma/\sqrt{N}$) of each mean based on a standard deviation, σ , of 0.06. $r=0.7784$ significant at 0.001 level.

geophysical properties and the metamorphism of the Massif all closely resemble that inferred for oceanic crust^{12,13}. Chemical evidence suggests ocean floor⁹ and volcanic arc¹⁴ affinities, but the geological evidence for a spreading origin is very strong indeed.

The mean TiO_2 for the Troodos samples was calculated on a log-normal basis as 1.00. Plotted on Fig. 1 this shows a slow spreading half rate of 0.5 to 1.2 cm yr^{-1} . Some independent information is available in this case. The rocks were erupted over a distance of 150 km, measured perpendicular to the spreading axis, during a period of normal magnetic polarity lasting almost 30 m.y. This gives a minimum half rate of 0.5 cm yr^{-1} which does not conflict with the result obtained here. The result also fits in with the interpretation of Moores and Vine¹⁵ of a slow spreading rate based on the abundant presence of chilled margins in the Troodos dyke swarm.

At present this method can only be used with confidence to distinguish fast and slow spreading ridges. With the use of more elements, data from a wider range of locations, more precise evaluation of spreading rates and a more detailed understanding of the petrogenetic variables involved, it may be possible to improve the spreading rate estimates considerably.

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High Resolution Laser Strainmeter

A new type of laser strainmeter is now operating in a disused railway tunnel at Queensbury, Yorkshire¹. It uses two helium-neon lasers operating at 633 nm, and has extremely high resolution and linearity. The frequency of one laser, called the slave laser, is locked to the length of a Michelson interferometer attached to the ground. The other laser, used as a reference standard, is stabilised by saturated absorption in iodine vapour²⁻⁵. A similar system has been reported by Levine and Hall⁶ using helium-neon lasers operating at the infrared 3.39 μm wavelength. For practical reasons it is easier to use visible light.

The evacuated Michelson interferometer has a long arm of 55 m, a short arm of 10 cm, and is illuminated by the slave laser. The mechanical and optical details of the interferometer have been described^{7,8}. The slave laser frequency is locked to the length of the interferometer by holding one fringe at the output of the interferometer through the application of a correction voltage to the piezoelectric transducer on which one laser mirror is mounted. The relationship between the frequency ν of the laser and the strain ϵ in the Michelson interferometer is

$$\nu = \nu_0(1/(1 + \epsilon)) = \nu_0(1 - \epsilon + \epsilon^2 - \epsilon^3 + \dots)$$

where ν_0 is the laser frequency when the strain is zero.

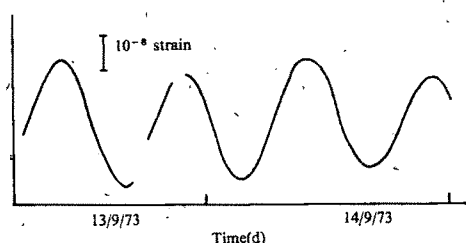


Fig. 1 Earth tides recorded by the laser strainmeter using an iodine absorption stabilised laser.

The light output from the slave laser is optically mixed with light from a frequency-stabilised reference laser to give a beat frequency equal to the difference in frequency between the two lasers. This is recorded digitally and on an analogue chart recorder. In the recording system the beat frequency is divided by 10^4 , and then enters a frequency counter which counts for 100 s every 2 min. Timing is provided by a crystal clock, and the least count corresponds to 2×10^{-13} strain. The resolution could clearly be increased to 2×10^{-17} strain, without altering the counting period, by omitting the divider and feeding the beat frequency directly into the counter. Increasing the length of the interferometer long arm would not change the resolution, although it would reduce the effect of errors introduced by poor coupling of the strainmeter mounts to the ground. Either of these changes could easily be made if required.

The beat frequency is constrained to remain between 10 and 90 MHz, which corresponds to a strain range of approximately

1.7×10^{-7} . When the beat frequency reaches either end of the range the slave laser frequency is stepped to bring the beat frequency back to the middle of the range. This extends the measurable range of strain even up to values which would mechanically damage the instrument. Theoretically, then, the relationship between laser frequency and strain is linear to less than 3×10^{-14} strain. This corresponds to a percentage non-linearity of $1.5 \times 10^{-5}\%$, which is much superior to that provided by any analogue system. In our instrument the linearity is, in practice, limited by the finite gain round the servo loop locking the slave laser frequency to the interferometer length. In principle this non-linearity could be reduced below the theoretical level.

The reference laser used in the system is one stabilised by saturated absorption in iodine vapour. Its frequency stability is better than 8×10^{-12} for the 100 s averaging time used in the beat frequency measurement^{4,5}.

A tidal record for two days is shown in Fig. 1 and there seems to be a relatively small amount of drift. Figure 2 shows a section of the record at high resolution. The record contains frequencies characteristic of microseisms at a reasonable amplitude.

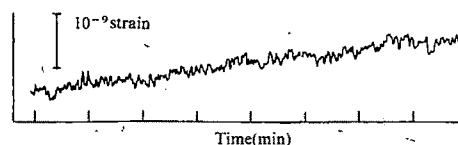


Fig. 2 Record at high resolution using the iodine absorption stabilised laser. Traced from the original chart recording.

This laser strainmeter will be used to study Earth tides and free oscillations of the Earth. The important features of the instrument are the high digital resolution and its exceedingly good linearity. These are very important when studying small signals in the presence of large signals of different frequencies. For example, the cusping of tidal peaks in frequency spectra^{1,9-11} may be due to real Earth effects, but it could equally be attributed to non-linearities in tide-measuring instruments.

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Late Aftershocks, Tectonic Stress and Dilatancy

THE focal mechanisms of micro-aftershocks occurring 3.5 yr after the Inangahua (New Zealand) earthquake of May 23, 1968 (magnitude 7.1), differ drastically from those of the main shock and early aftershocks and are in apparent conflict with the known tectonic stress. This anomaly calls for an explanation as microearthquakes are widely regarded as reliable indicators of tectonic stress. A possible explanation is suggested by the dilatancy hypothesis, which has recently received much attention as a promising basis for earthquake prediction¹⁻⁴.

The usual type of aftershocks, in which the mechanism is like that of the main shock, has already been linked with the flow of pore fluid within the main source region⁵. In the occasional earthquake that involves overshoot, the subsequent deformation in the reverse sense seems to occur by stable sliding without aftershocks⁶. The change in aftershock mechanism observed at Inangahua could possibly have resulted from a delayed outflow of pore fluid from the main source region into the surroundings.

The Inangahua earthquake and early aftershocks have been described by Adams and Lowry⁷. The main shock had epicentral coordinates 41.77° S, 172.01° E, with depth in the upper crust (assigned depth 12 km). Through a 40 d period following the main shock, 809 aftershocks were located including twelve of magnitude 5 or greater. The epicentres were nearly all situated within an elliptical area about 45 km by 25 km. Location was aided by readings from two temporary seismographs which were installed in the vicinity after the main shock. The nearer of these was used for depth control; computed depths ranged from 5 km to 19 km.

The nature of the tectonic stress in the region is known from surface faulting both in the 1929 Murchison earthquake and the Inangahua earthquake⁸ and also from first motion studies^{7,9}. Fig. 1*a* shows a more extensive compilation of first motion data for some well observed and widely distributed early aftershocks in the Inangahua sequence, together with a replotting of published data⁷ for the main shock. The nodal plane which strikes N 19° E and dips 44° E has an orientation close to that of the known faults in the region; the movement on it is dominantly thrust with a small left-lateral component.

A very different type of faulting was consistently indicated by aftershocks observed about 3.6 yr after the main shock. These were recorded over the period January 4 to 19, 1972, in the course of a regional microearthquake survey which included the area around Inangahua. By means of four portable recorders, numerous earthquakes with magnitudes up to $M_L = 3.1$ were found to be concentrated within an elliptical area situated similarly to the area of the early aftershocks but with the somewhat reduced dimensions 40 km by 15 km. This continued occurrence of aftershocks is to be expected for an earthquake of the magnitude of the Inangahua main shock. Computed depths ranged from 1 km to 20 km, not significantly different from those of the early aftershocks. A composite plot of the first motions of all well observed shocks in this late period is shown in Fig. 1*b*. These shocks were also well distributed through the aftershock volume. One of the nodal planes again has a strike (N 27° E) close to that of the surface faulting, but the dip is 78° NW. Choosing this as the most likely fault plane one finds that normal faulting was dominant, again with a small left-lateral component.

Between the early and late aftershocks, the fault movement has thus changed from thrust to normal and the dip of the fault planes has swung through about 60°. As the internal consistency of each first motion plot is rather high, it seems that at each stage the seismogenic condition of the aftershock volume was substantially uniform. Some positive explanation is needed for the drastic change in mechanism. In a region where the tectonic stress is compressive, it is difficult to see how pervasive normal faulting can set in apart from recovery after

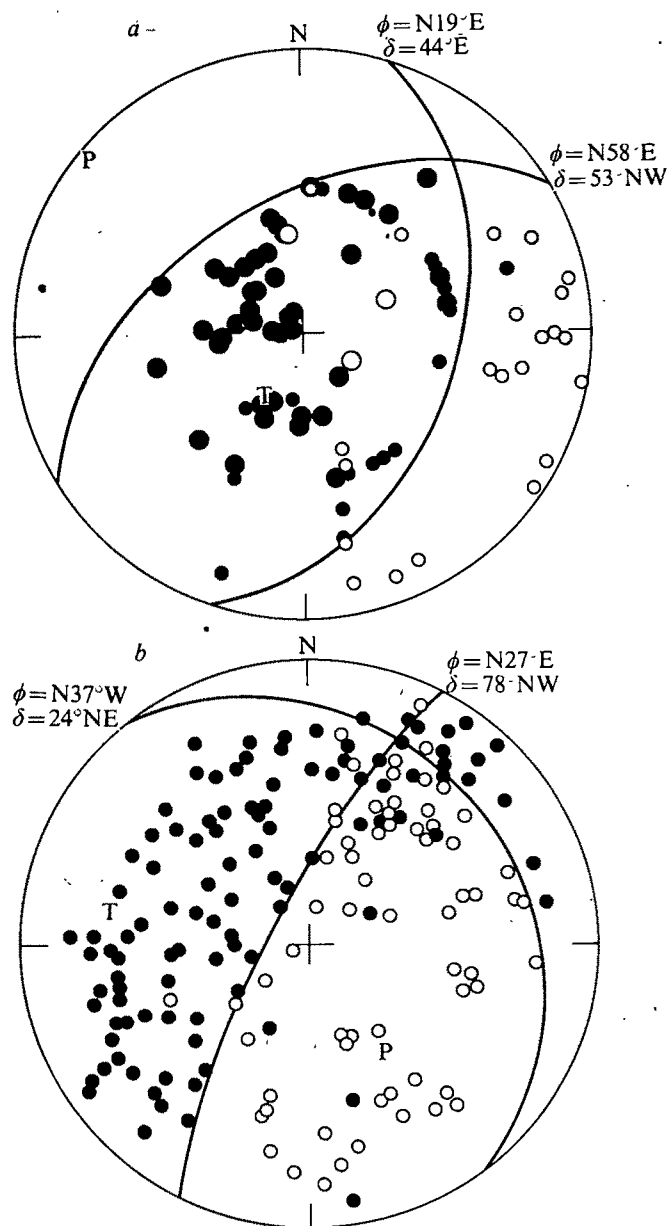


Fig. 1 Composite focal mechanism diagrams of the Inangahua earthquake sequence on equal-area stereographic projections of the lower focal hemisphere. Each nodal plane is specified by a strike ϕ and a dip δ . Idealised axes of compressive and tensional stress are indicated by P and T respectively. *a*, Main shock (large circles) and early aftershocks (small circles); *b*, late aftershocks. ●, Compressions; ○, dilatations.

overshoot, unless the tectonic stress is reduced to a low level and material is somehow removed at depth.

An earthquake and its aftershocks serve in general, of course, to reduce the tectonic stress, and there is no great difficulty in supposing a low stress level to have been reached throughout the source region at the time of the late aftershocks. In most shallow earthquakes, as is well known, there is incomplete stress release. Fitch and Scholz⁶ have characterised the motion in this case as overdamped, and the motion when overshoot occurs as underdamped. In these terms we propose that the motion in the main Inangahua earthquake was slightly overdamped. As for the removal of material at depth in the period following an earthquake, this would often be a consequence of pre-earthquake dilatancy.

On the dilatancy hypothesis there is an inflow of pore fluid to the source region before an earthquake. One effect of the earthquake itself, then, is to reduce the dilatancy spaces and thus increase fluid pressure, and if the level of pressure in the

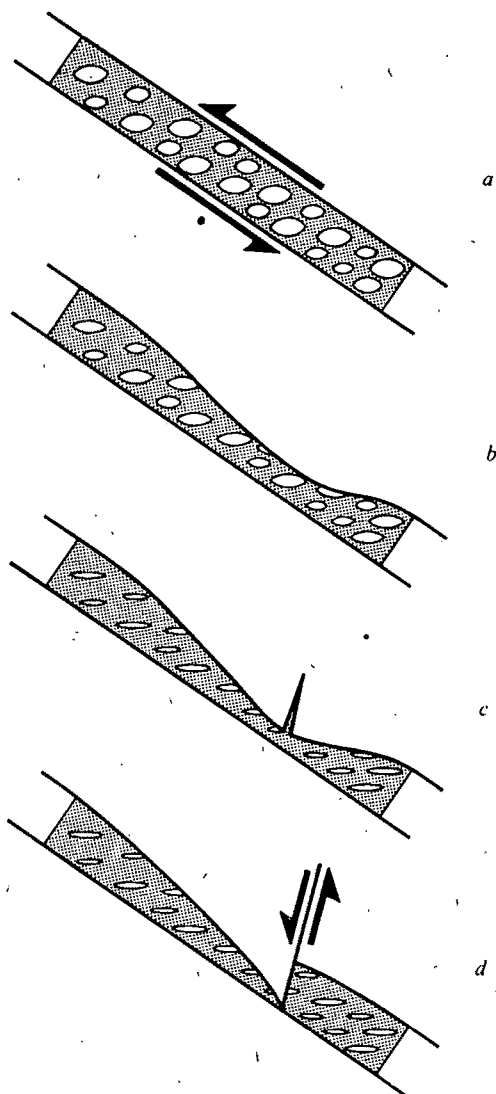


Fig. 2 Schematic representation of change from thrust faulting in main shock and early aftershocks to normal faulting in late aftershocks, as a delayed effect of pre-earthquake dilatancy. *a*, In a pocket containing a high concentration of dilatancy cracks, thrust faulting reduces the tectonic stress to a low level and raises the fluid pressure to a maximum. *b*, Fluid is forced out of the dilatancy cracks and the overlying rock sags. *c*, Further outflow, further sagging, and hydraulic fracturing. *d*, Normal faulting on a steeply dipping plane.

surrounding region is thereby exceeded fluid will begin to be forced out of the source region again⁴. In the broadest terms the observed normal faulting in late aftershocks might be attributed to subsidence following such an outflow of fluid. This would not, however, explain the change in the orientation of the fault plane. Unless there is inherent in the rock a second plane of weakness which is especially favourable to normal faulting, one might expect at first glance that slip should occur on the same fractures that were involved in the main shock and early aftershocks, as in the case of recovery after overshoot. The following simple considerations suggest differently, however, if one invokes the dilatancy concept.

Presumably the dilatancy cracks would be concentrated to some extent in sheet-like pockets along the fault surfaces on which movement occurred in the main shock and early aftershocks. Such a pocket is depicted schematically in Fig. 2; it could be small or extensive. Immediately after the main faulting the fluid would be at maximum pressure and would provide maximum support for the overlying rock (Fig. 2*a*). If the pressure exceeded the ambient value and outflow subsequently occurred, this support would be reduced and the overlying

rock would tend to sag (Fig. 2*b*). Hydraulic fracturing would then tend to develop at points of greatest curvature (Fig. 2*c*), with consequent normal faulting (Fig. 2*d*). The strike of the normal fault would be about the same as for the main faulting, but the dip would be in the opposite azimuth, and steep. This is as observed. We can thus account for the large change in the orientation of the fault plane without introducing the *ad hoc* postulate of a second and conveniently oriented plane of inherent weakness in the rock.

The precursory effects associated with dilatancy, according to Scholz *et al.*⁴, occupy an interval of time which is related to the magnitude of the consequent earthquake. This is the time between the rapid dilation of cracks and the eventual raising of fluid pressure to fracture level by inflow; it is a function of the pressure change, the ground permeability, and the volume of the source region. For the Inangahua earthquake ($M=7.1$) the time would have been about 7.5 yr. Since a roughly similar time should be required by the outflow process it is satisfactory that the observed effect was present after 3.6 yr. The small tectonic stress evidenced by the left-lateral component could have been stress that was left unrelieved by the main shock and early aftershocks, or stress beginning to build up again for the next cycle.

This mechanism for generating microearthquakes as a result of fluid outflow would have no counterpart during the inflow stage. At that time, with the region under compression, the rock would be progressively strengthened as dilatancy reduced the pore pressure. In a region of compressive tectonic stress and, apart from overshoot, it is only late in the stage of fluid outflow that overall conditions would be in any way favourable to normal faulting.

The contrast in focal mechanism between the early and late earthquakes of the Inangahua sequence can thus be interpreted as an effect of dilatancy. This proposal is susceptible to test by the observation of late aftershocks following other main shocks that are due to thrust faulting. If the motion is slightly overdamped and is followed by an outflow of pore fluid, the mechanism of late aftershocks will be more or less strongly influenced by gravity. In view of the long time constant that is attributed to the migration of pore fluid it is not surprising that such an effect should have escaped notice hitherto.

The observations reported here show that a stress orientation indicated by microearthquakes occurring over a substantial area may be very different from that of the tectonic stress. This may be an isolated anomaly with some *ad hoc* explanation. If the dilatancy hypothesis is valid, however, and applicable to events such as that at Inangahua, the explanation proposed above may have some generality.

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Interstadial Site on the Island of Lewis, Scotland

A THIN layer of organic detritus found beneath glacial till in north Lewis has been radiocarbon dated to $27,333 \pm 240$ BP. This dating is an important contribution to an appreciation of British glacial chronology. The significance of the organic bed is enhanced by its yielding sufficient pollen for analysis.

The tabular surface of the Tolsta Head peninsula in north Lewis (Fig. 1) is covered with patches of glacial till. The surface is everywhere mantled with peat. In a shallow depression on the south side of the headland a freshly-eroded cliff section at NB 5572 4682 showed the till resting on laminated silt and organic lake detritus over a distance of 17 m. The stratigraphy at the point of sampling is shown in Fig. 2. On the basis of the interbanding of the finely comminuted rootlets with silt, the organic deposit was classified as lake detritus,

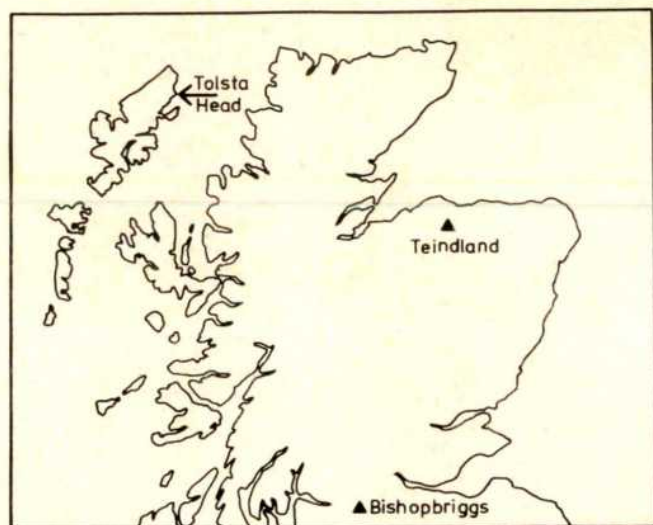


Fig. 1 Site location.



Fig. 2 Organic layer at Tolsta Head.

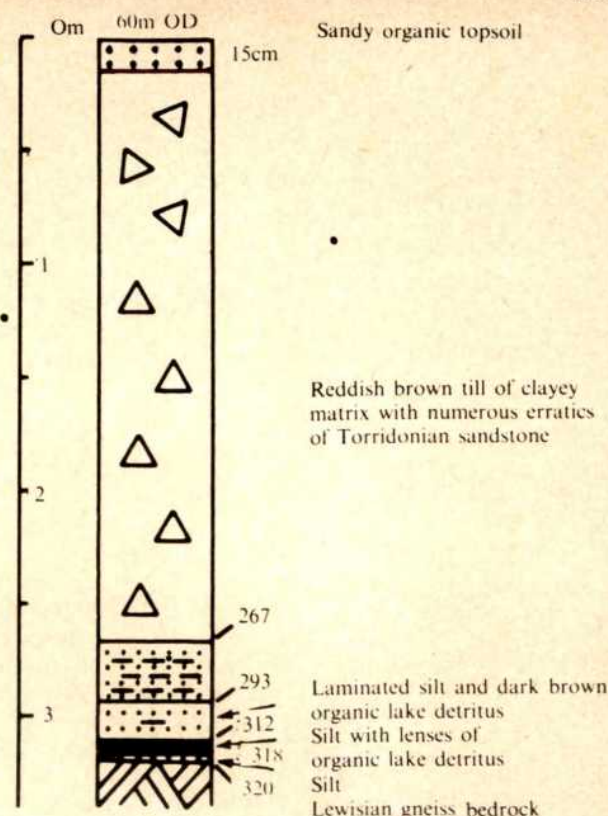


Fig. 3 Stratigraphic column.

which probably accumulated in a temporary lake basin. The bedrock at the site slopes slightly towards the NE. The stones in the glacial till, however, show a preferred SE orientation and dip. Therefore the glacial deposit is unlikely to be of soliflucted origin.

A block from the topmost 15 cm of the laminated silt and lake detritus was collected and submitted for radiocarbon dating to the Scottish Universities Research and Reactor Centre, East Kilbride. The organic material provided an age of $27,333 \pm 240$ BP (SSR-87). The date is based on the Libby half-life of $5,570 \pm 30$ yr. There was no evidence of modern contaminants. The new date is remarkably close to two dates on the Scottish mainland. A buried soil horizon underlying till and outwash gravel at Teindland (Fig. 1) was dated at $28,140$ BP¹. The other is a date of $27,550$ BP for a water-worn bone of a woolly rhinoceros, which was found incorporated in fluvioglacial sands and gravel at Bishopbriggs² (Fig. 1). Sissons³ has suggested, because the site at Bishopbriggs is not far from the central part of the former Scottish ice sheet, that the whole of Scotland may have been ice free at that time. Similar dates to those from Scotland have been recorded in the English Midlands⁴, the Netherlands and Austria⁵.

Treatment of the deposit with hydrofluoric acid produced sufficient pollen for analysis. The pollen was in a good state of preservation and permitted counts of between 300 and 500 grains per level. The pollen and spore types in the diagram (Fig. 4) are expressed as a percentage of the land pollen sum. The high frequencies of grass pollen and light-demanding herbaceous species such as *Calluna vulgaris*, Compositae and Ranunculaceae indicate an open vegetated landscape. This is further suggested by the presence of juniper, which has a preference for open vegetation⁶. The willows may have occupied damper soils adjacent to a sedge-fringed lake, or perhaps formed a more extensive shrub element, interspersed with juniper over the surrounding area. The isolated grains of *Pinus* and *Picea* must almost certainly have arrived by long-distance wind transport.

The pollen record provides an indication of the climate of

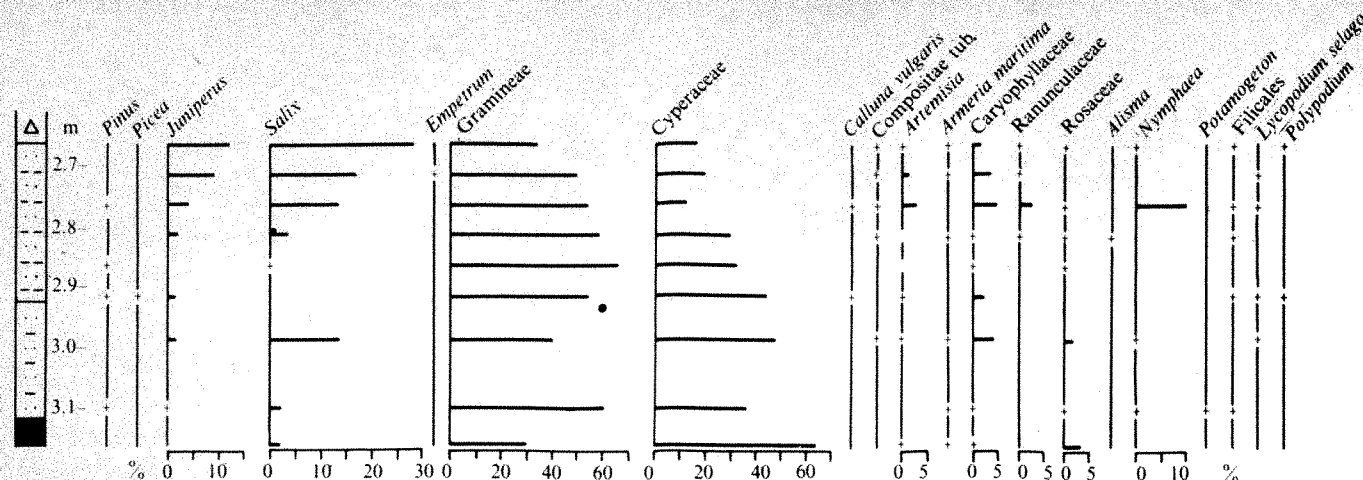


Fig. 4 Pollen diagram from Tolsta Head. +, Indicates less than 2% of sum of land pollen. Note the differing scales for Gramineae and Cyperaceae. Stratigraphic symbols as in Fig. 3.

the time. The taxa present have been found in late-glacial deposits from Britain^{7,8} and mainland Europe⁹. This observation and the lack of tree pollen do not, however, necessarily indicate a severe stadial climate. *Nymphaea* is a genus recorded in late-glacial deposits but is favoured by more temperate conditions¹⁰. *Armeria maritima* is intolerant of extreme cold and is characteristic of areas with an oceanic climatic regime¹¹. The pollen spectra are not inconsistent with the cool maritime climate of Lewis. The increased representation of the warmth-loving juniper¹² in the upper section of the diagram might be considered anomalous before the impending glacial advance responsible for the overlying till. Although the species possesses a wide ecological amplitude¹³, a possible interpretation is that the deposit has been truncated by glacial erosion. The profile may therefore be incomplete.

The significance of the dated deposit lies in its stratigraphic context. The overlying glacial till contains numerous erratics of Torridonian sandstone, a rock type alien to the lithological assemblages of the Outer Hebrides. The abundance of these erratics in the till suggests deposition by an ice mass which had moved over at least part of the Minch. This suggestion is supported by two other lines of evidence. Till-fabric analysis on the site revealed a predominant stone orientation of 50° W of N to 50° E of S and dip towards the SE. Also, till with shell fragments is exposed in a coastal section 1.2 km west of the site¹⁴. Other glacial deposits containing Torridonian sandstone erratics and broken shells, but of a more complex nature, have been found on the Eye peninsula and at the northern tip of Lewis^{15,16}.

The organic layer has thus produced a third date in support of interstadial conditions in Scotland at 27,000 to 28,000 BP. Pollen analysis gives an indication of the vegetation and climate at this time. The stratigraphic sequence at the site provides evidence for the presence of glacier ice at Tolsta Head after about 27,330 BP.

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Multiple Discriminant Screening Procedure for Test Ban Verification

A DECADE of research has led to a well defined capability for the seismological method of verification of compliance with a ban on underground nuclear explosions. Whatever political form the treaty will eventually have, it is generally agreed that decisions concerning violations will be national decisions. Recent presentations to the Conference of the Committee on Disarmament in Geneva¹⁻⁴ lead us to consider in some detail utilisation of the seismological discrimination experience in a national operational verification procedure. The thrust of the sample operational procedure to be described depends on an acceptance of the fact that detailed consideration of clandestine explosions, or evasion tactics in general, is futile until all natural seismic activity can be identified down to the required seismic magnitude or equivalent explosion yield. Thus, the operational procedure becomes an earthquake screening process that can be tested in simulation in advance of the Test Ban Treaty.

The seismic region chosen for a simulation is a major portion of Eurasia (Fig. 1) and the monitoring nation can be assumed to be Canada, although with the data exchange procedures inherent in the scheme it could be any nation. The seismic events considered are from the Lincoln Laboratory, MIT bulletin for the 29-day 'International Seismic Month' (ISM)⁵, the most comprehensive global seismic bulletin assembled to date on the basis of teleseismic observations; the number of events in each of five regional blocks is shown in Fig. 1.

The total of 291 events, shown in cumulative distribution in Fig. 2a, are subjected to three types of earthquake screening: (a) those with epicentres at sea, (b) those with focal depths greater than the maximum feasible drilling depth, and (c) those that are earthquake-like by one or both of the $M_s:m_b$ and P-wave discrimination criteria. The result of this screening is shown in all combinations as histograms

in Fig. 2*b* to *e*. The location screening assumes that nuclear test emplacement is impractical from a location at sea and events are screened as earthquakes if their epicentres are at sea by at least the largest epicentre error ellipse semi-axis. The result is 152 earthquakes at sea (Fig. 2*b* and *c*) and 139 events with epicentres on land or within the epicentre error of a land mass (Fig. 2*d* and *e*). The focal depth screening assumes that nuclear test emplacement is impossible at depths greater than maximum feasible drilling depths, assumed here to be 10 km. Events are screened as earthquakes if their computed focal depths are greater than the largest hypocentre error ellipsoid semi-axis plus 10 km. The independent result of this screening is 158 deep events (thus earthquakes) shown in Fig. 2*b* and *d* and 133 events with depths less than 10 km or with computed depths within the hypocentre error of this depth. (Note that the word 'deep' as used here refers to deeper than 10 km, rather than the more standard usage for earthquake depths.) The combined result is eighty-eight events (30% of the total) in Fig. 2*e* that remain for further consideration as possible explosions.

To screen these events using discrimination criteria, we have used a formal two-group discrimination analysis⁶. In brief, accumulated experience with the $M_s:m_b$ criterion⁷ and the Yellowknife array P-wave criterion^{8,9} for the Eurasian region for earthquakes and underground explosions are used as design sets to define multi-parameter discrimination functions that optimise the separation between the explosion and earthquake populations. A decision level is chosen in the multi-parameter hyperspace to screen earthquakes with near certainty. For each of the ISM events for which discrimination results are available, the position in hyperspace is computed and an earthquake decision made if the event falls to the earthquake side of the decision level. For the $M_s:m_b$ criterion, which is two-dimensional, this decision level can be presented visually with reference to the standard $M_s:m_b$ plots: the earthquake decision is made for events with $M_s \geq 1.5 m_b - 3.4$. This is intended to be a cautious earthquake decision level and, for example, requires M_s half a magnitude greater than those of the most earthquake-like explosions in the plot of Marshall and Basham⁷.

An equivalent procedure is employed for the P-wave criterion for which the hyperspace is twelve-dimensional. The Yellowknife array P-wave discriminant utilises the shorter duration, impulsive nature of explosion P waves, as measured by seven parameters in the time domain, and the greater relative high frequency content of explosion P waves, as measured by five parameters in the frequency domain, to distinguish them from earthquake P waves. For this

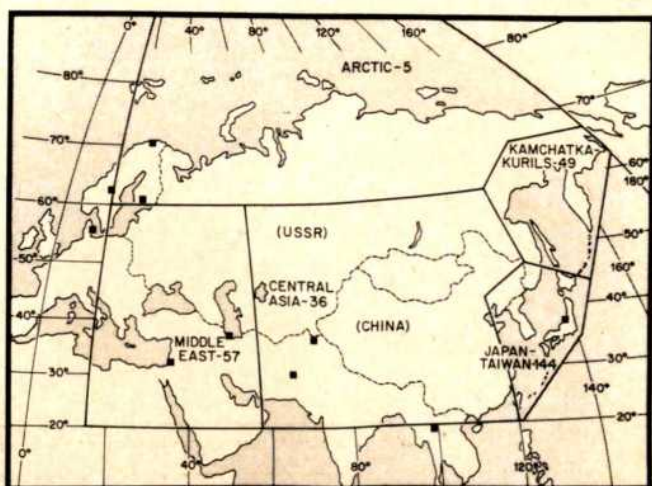


Fig. 1 International Seismic Month seismic event distribution in five Eurasian geographic blocks. Solid symbols show locations of Eurasian seismograph stations used for M_s magnitudes.

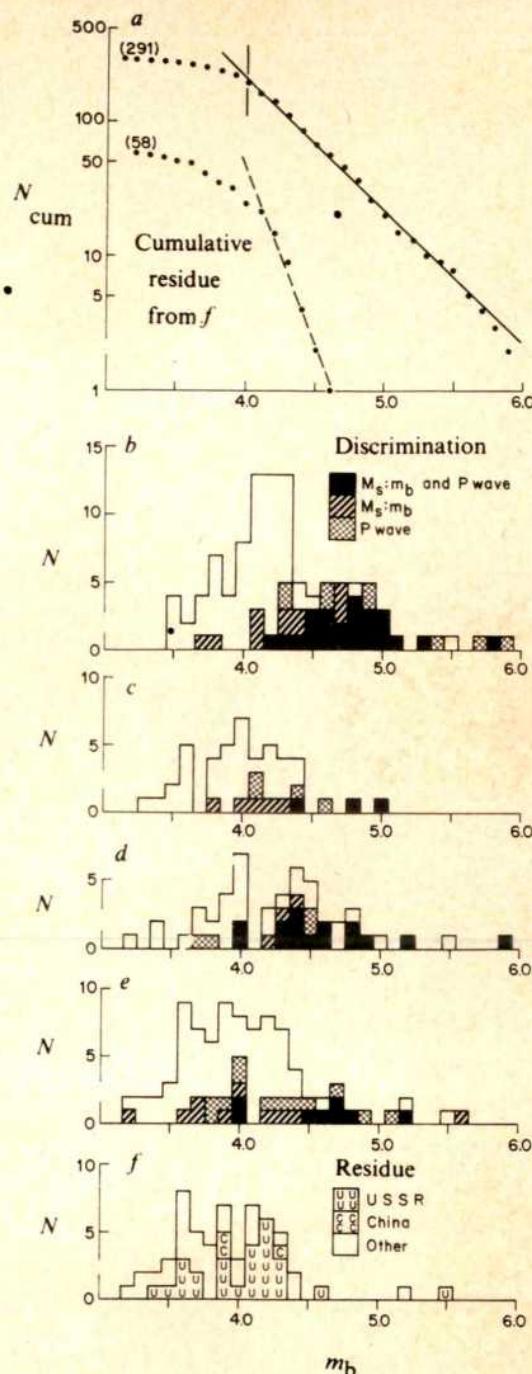


Fig. 2 Eurasian earthquake screening results for the International Seismic Month. *a*, Total cumulative event distribution illustrating bulletin is 90% cumulative complete at $m_b 4.0$; *b*, events with epicentres at sea and focal depths greater than 10 km; *c*, at sea and shallower than 10 km; *d*, on land and deeper than 10 km; *e*, on land and shallower than 10 km; *f*, final screening residual events. Earthquake decisions by discrimination criteria are shown as shading in *b* to *e*. Residual events are shown in cumulative distribution in *a*.

application, the decision level is chosen in a similarly cautious manner with respect to experience with the most earthquake-like explosions in the large population studies (ref. 8 and F. M. A. and H. Israelson, in preparation).

As shown by the histogram shading in Fig. 2*b* to *e*, fifty earthquake decisions can be made on the basis of the $M_s:m_b$ and P-wave criteria together, thirty on the basis of the $M_s:m_b$ criterion alone and twenty-nine on the basis of the P-wave criterion alone. All but eight, ten and twelve of these decisions, respectively (those in Fig. 2*e*), are redundant,

the other events having previously been screened by location or depth. The residue of events that have not been classified as earthquakes to this point in the procedure is shown in Fig. 2f.

It is clear from Fig. 2 that the probability of earthquake decisions on the basis of the discrimination criteria decreases rapidly at magnitude below $m_b 4.5$. In addition, the ISM bulletin becomes incomplete as the magnitudes decrease much below this value: being 90% cumulative complete at $m_b 4.0$, it is 90% incremental complete at about $m_b 4.3$. The threshold of this monitoring experiment has therefore been set on an equivalent level, say $m_b 4.3$, by both the event detection/location capability and the earthquake identification capability. To continue the experiment further in terms of simulated verification would require some assumptions about the goals of the procedure in a treaty situation. For example, if $m_b 4.3$ were the desired threshold capability, then the ten events in Fig. 2f with magnitudes $\geq m_b 4.3$ would be treated exhaustively to attempt to establish their identity. This will not be attempted here, but some general comments are of value. The $m_b 5.5$ residual event was in Eastern Kazakh and is identified as an explosion by all criteria; such a larger explosion at the principal Soviet test site is largely irrelevant to discussions of a treaty situation. Three of these ten events are believed to have overestimated magnitudes; two have observable depth phases that suggest they are deeper than 30 km; we have no additional information for the other four, each at $m_b 4.3$.

Table 1 Projected Annual Numbers of Eurasian Earthquakes

Category	$\geq m_b 4.0$	$\geq m_b 4.5$
(1) Total for Eurasian region considered	2,800	880
(2) USSR land mass epicentres	450	140
(3) China land mass epicentres	140	50
(4) Total screening residue	630	38
(5) USSR residue	315	(13)
(6) China residue	(13)	(0)

In addition to the actual numbers of events available for the 29-day period in the above screening process, the recurrence curve (Fig. 2a) for the events is sufficiently well defined to allow some projections of annual numbers of events that would require treatment by such a procedure. Comparisons of annual projections of these events with equivalent data presented by Evernden⁹ and Anglin¹⁰ demonstrate that the ISM is adequately representative of average Eurasian earthquake rates. As the ISM bulletin is the most comprehensive one to date based on the m_b scale, it probably provides the most accurate available estimates of numbers of land mass earthquakes in the Soviet Union and China in the m_b range ≥ 4.0 . For the annual occurrence rates given in Table 1, the projected 100% occurrence rates for the ISM period are simply multiplied by 365/29.

Some indication of how an operational verification scheme intended to monitor the Soviet Union and China can treat these, say, 600 annual land mass events ≥ 4.0 is available from the 'shallow land mass' residue in Fig. 2f. The residual events, with the $m_b 5.5$ explosion removed, are plotted in cumulative form as an inset in Fig. 2a. As each of the location, depth and discrimination screening criteria is removing events in a magnitude-dependent and region-dependent way, there is no certainty that the residue will have an equivalent recurrence distribution. If, however, the straight line shown is accepted as representative of the residue, some projections can be made, and are listed as categories 4, 5 and 6 in Table 1. An interpretation that can be made of these projected residue events is to assume that the screening procedures outlined here applied in a routine way by the monitoring nation; the residue then represents those events that must be subjected to additional analysis in

order to establish their sources as being earthquakes or explosions.

In summary, it is important to note that the ISM bulletin used for the simulation is increasingly incomplete at magnitudes below $m_b 4.3$, even though its compilation made exhaustive use of the best P-wave detection facilities in existence. Thus, any nation requiring a verification (earthquake screening) capability at about $m_b 4.0$ must first deploy additional facilities to detect and locate the events. If a nation were to monitor the Soviet Union and China with some substantially increased facilities over those that currently exist and concern itself with all events ≥ 4.0 , it must assess about 600 events per year with land mass epicentres. It seems very unlikely that, using teleseismic techniques, discrimination criteria will be devised to screen confidently all of these events as earthquakes. If an explosion is detonated under some evasion scenario whereby either the explosion cannot be assessed as an independent seismic event or it is screened as an earthquake using procedures such as those described above, then the seismological method will not note a violation of the treaty. These are simplified statements of the limitations inherent in the seismological method.

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New Spin Structure in an Amorphous Ferric Gel

AMORPHOUS materials have no preferred crystal axes, but it might be thought that shape or strain could define an anti-ferromagnetic axis in a compound containing a large concentration of magnetic ions with negative nearest-neighbour exchange interactions. We have studied such an amorphous compound, and find an ordered state where spins are coupled with their directions statistically distributed within a very fine particle. This spin structure is quite different from normal antiferromagnetism, although there are some similarities in the magnetic properties.

The material studied was precipitated near freshwater springs on Caton Moor, Lancashire; 97% of the inorganic fraction was a ferric gel with empirical formula $\text{Fe}(\text{OH})_3 \cdot 0.9 \text{H}_2\text{O}$, and

it was mixed with 30% of organic matter and 2% of silicate minerals. No evidence for crystallinity was found by X-ray or electron diffraction, and the material was almost completely dissolved by acidified ammonium oxalate, a treatment which extracts only the non-crystalline fraction¹. Details of the characterisation and magnetic properties of the amorphous gel are to be published. The main features of its magnetic behaviour may be summarised as follows. Below about 10 K it is clear from the existence of a remanence and from the Mössbauer spectrum of Fig. 1a that there is an ordered magnetic structure. The moment obtained by extrapolating the linear portion of the 1.6 K magnetisation curve (above 50 koersted) back to 0 koersted is 8.6 e.m.u. per g of gel. The Mössbauer spectrum becomes a simple quadrupole doublet above 20 K, yet Curie-Weiss paramagnetism is found only above 100 K. The gel is in the form of ultra-fine particles (≤ 100 Å) and the magnetisation curves, plotted as a function of H/T , superpose between 30 and 80 K. They may be represented by a Langevin function with a spontaneous moment of 7.2 e.m.u. g^{-1} , in satisfactory agreement with the 1.6 K extrapolation, and a moment per particle of $73 \mu_B$ (ref. 2). In other words, the collapse of the Mössbauer hyperfine splitting above 10 K corresponds to the unblocking of the superparamagnetic fine particles, and the true magnetic ordering temperature is higher, about 100 K.

Here we are concerned with the spin structure of these amorphous fine particles. If they were antiferromagnetic (Fig. 2b) the spins of a particle would all lie in a line. The particle's weak moment would arise from the statistical imbalance of up and down spin, and would be parallel to the spins. Alternatively, the weak moment would conceivably result from a slight canting of the sublattices, and would then be almost perpendicular to the spins, as in $\alpha\text{Fe}_2\text{O}_3$. Which configuration, if either, is correct can be decided from Mössbauer spectra in applied fields, shown in Fig. 1. Fields of 10 and 50 koersted were chosen which almost ($5.8 \text{ e.m.u. } g^{-1}$) or completely ($12.8 \text{ e.m.u. } g^{-1}$) saturate the weak moment. In zero applied field, lines 2 and 5 comprise $34 \pm 2\%$ of the total absorption,

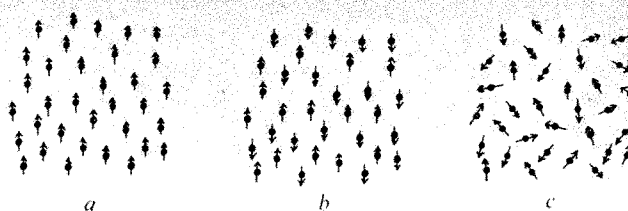


Fig. 2 Possible spin structures for an amorphous compound. a, Ferromagnetic; b, antiferromagnetic; c, sperrimagnetic.

as is usual for the random alignment of spins relative to the γ -ray direction found in a multiparticle sample³. When the field is applied parallel to the γ direction the absorption in lines 2 and 5 would be 0% if all the spins were parallel or antiparallel to the field, as expected if a weak moment arising from the first spin configuration was saturated. Also the spectrum should double, or at least show structure, at 460 ± 50 in Fig. 1c as the applied field adds to one sublattice and subtracts from the other. Conversely, if the spins were almost perpendicular to the field, as expected for the second configuration, or if a spin flop had occurred, the absorption in lines 2 and 5 would be 50% of the total. The calculated spin flop field actually is 100 koersted for these particles, much greater than the applied fields. In Fig. 1 it is obvious that neither of the above possibilities is the correct one. The spectrum is hardly changed by the applied field, 33% of the absorption remaining in lines 2 and 5 in 10 koersted, and 29% in 50 koersted. There is no doubling of structure, but only some broadening of the outer lines. In summary, the data are not consistent with any kind of antiferromagnetism in these fine particles, but they show that the spins within a particle are statistically distributed relative to the direction of their resultant moment.

Such a configuration, with the spins fixed relative to each other but possessing no overall preferred direction, is illustrated in Fig. 2c. It is termed 'sperrimagnetic' (Greek διασπειρω, I scatter), and although it has only been possible here to demonstrate its existence in ultrafine particles because they have a resultant moment relative to which the other spin directions can be measured, it is probably a fairly common phenomenon in amorphous compounds.

The resultant moment of a particle containing N ions, each of moment m , pointing in random directions is $\sqrt{N}m$. The value of the hyperfine field at 4 K (460 koersted) shows that the ferric moment is only a little less than its ionic value of $5 \mu_B$. From the superparamagnetic magnetisation curves we deduce that each particle contains an average of 635 formula units, and the predicted moment is thus $\sim 126 \mu_B$, rather larger than observed. The difference can, however, be accounted for as follows. The Curie constant gives an unexpectedly small effective moment of $3.68 \mu_B$, but this is also observed in synthetic gels where it is explained by the equilibrium concentration of a ferric dimer, built into the gel structure as it is precipitated⁴. Thirty-eight per cent of the iron is thus coupled rigidly antiparallel to an iron neighbour and will not contribute to the net moment. The predicted particle moment is now $78 \mu_B$, in excellent agreement with the observations.

There are some similarities between sperrimagnetism and the magnetism of alloys such as Cu Mn or Au Fe which are known as mictomagnetic alloys or spin glasses. A mictomagnet^{5,6} is also characterised by the freezing of spin orientations at low temperatures without any long range spin order, but within this matrix there are clusters of short range order, which possess giant moments. The magnetisation in a zero field cooled specimen passes through a maximum near the temperature where the remanence goes to zero, and the hysteresis loop is considerably displaced by field cooling. Neither of these effects were observed in our material. The same alloys are known as spin glasses at lower concentrations of the magnetic

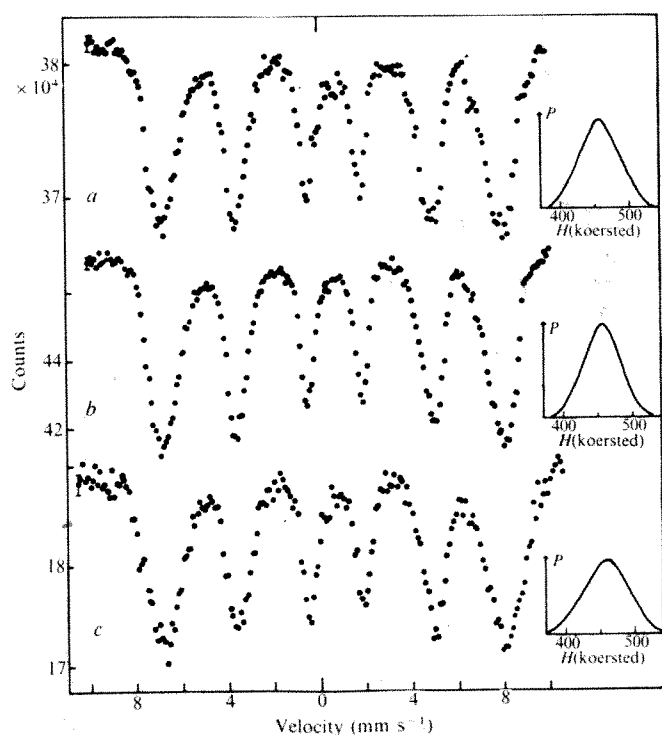


Fig. 1 Mössbauer spectra of amorphous $\text{Fe(OH)}_3 \cdot 0.9 \text{ H}_2\text{O}$ at 4.2 K in a field of 0 koersted (a), 10 koersted (b) and 50 koersted (c) applied parallel to the γ direction. The insets show the hyperfine field probability distributions, $P(H)$.

solute atoms. They are characterised by both ferromagnetic and antiferromagnetic coupling, but it has recently been emphasised that any understanding of the microscopic structure of the ordered state is still very unclear⁷, particularly concerning the formation of clusters.

Finally, we consider possible reasons for the random orientations of the spins in a sperimagnet. (The orientations are random in a volume containing $\sim 10^2$ spins; there is nonetheless a net antiparallel correlation in the shell of first neighbours.) A possible explanation might be that the single ion anisotropy is very large for certain cations (though not for Fe^{3+}) in the irregular ligand coordination polyhedron, and the spin direction is thus fixed by the local charge environment. It is more likely, however, that the spin directions are determined by the balance of exchange interactions, such as give rise to the canted spin structures in diamagnetically substituted ferrites⁸ and the disoriented spin structure suggested for the surface of ultrafine $\gamma\text{Fe}_2\text{O}_3$ particles^{9,10}.

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Optical Elastohydrodynamics at Extreme Pressures

THE theoretical predictions of Dowson and Higginson¹ concerning the size of the lubricant film generated in rolling-bearing line contacts have been adequately confirmed over a fairly large range of pressures and for a wide selection of temperatures, speeds and fluids (see, for example, ref. 2). The theory has been extended to include point and elliptical contact conditions³⁻⁵ and various aspects of non-Newtonian fluid behaviour (see, for example, ref. 6). Lately, however, there has been a need to test the predictions at much higher pressures as the loading in modern bearings constantly increases. Since optical elastohydrodynamic techniques^{7,8} have been limited to a pressure of about $7 \times 10^8 \text{ N m}^{-2}$ (100,000 pound inch⁻²) by the use of glass as one lubricated element, this investigation has largely fallen to the X-ray method⁹. This technique has been doubted by some workers although it has generally reaffirmed the data obtained with earlier methods of film thickness measurement. Unfortunately,

recent results¹⁰ with this method differ greatly from theory. Film thicknesses have been found an order of magnitude below predicted values at pressures of $2 \times 10^9 \text{ N m}^{-2}$, and the dependence on load has been generally too great. It is therefore uncertain whether this is a failure of the Dowson and Higginson type of theory or of the X-ray method itself.

The work outlined here concerns an extension of optical elastohydrodynamic film thickness measurements in pure rolling to pressures of over $2.0 \times 10^9 \text{ N m}^{-2}$. This has been achieved using a lubricated sapphire disk, over which rolls a highly polished 1-inch diameter tungsten carbide ball. This replaces the combination of steel on glass used by previous workers⁷ but is otherwise very similar.

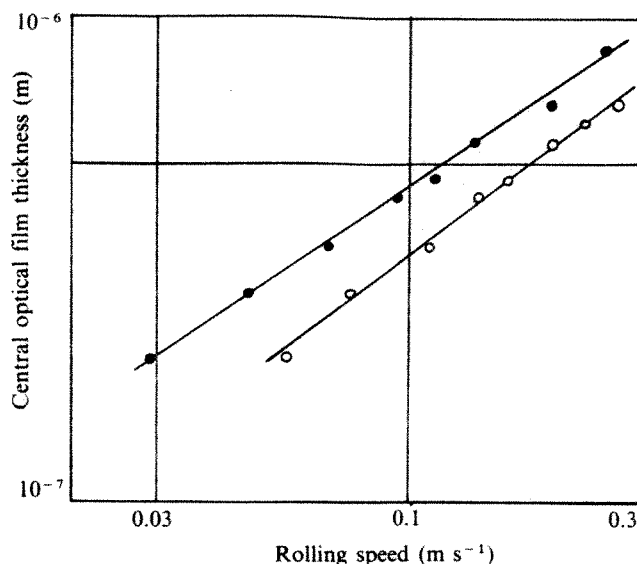


Fig. 1 Typical film thickness/speed results (fluid 3). Maximum Hertz stress: ●, $8.4 \times 10^8 \text{ N m}^{-2}$ (1.2×10^5 pound inch⁻²); ○, $20.7 \times 10^8 \text{ N m}^{-2}$ (3.0×10^5 pound inch⁻²).

Three fluids have been examined: (1) a synthetic paraffin, as used in ref. 10; (2) naphthenic mineral oil base stock; and (3) fluid 2 plus 10% W paraffinic heavy resin. They were tested at nine loads to cover the range of pressures from 0.8 to $2.0 \times 10^9 \text{ N m}^{-2}$. For the time being the temperature used has been ambient. The experimental method was to increase the rolling speed from zero while observing the point contact with chromatic interferometry. At each of at least eight set film thicknesses the rolling speed was measured. The results are displayed graphically as in Fig. 1. The variation of film thickness with load, which is in question, was obtained by drawing lines at chosen rolling speeds and reading off the value of film thickness at the intercept for each load. The results obtained by this method are given in Fig. 2. They show an almost linear variation of film thickness with load over the whole range, according to the relationship

$$h \propto W^{-a}$$

with a as given. Owing to the fact that point contact pressure increases as the cube root of the load, an estimate of error in the pressure data is about $\pm 10\%$ at low loads but better than $\pm 1\%$ at high loads. On the other hand, at high loads there is an unavoidable rise in temperature of the fluid at the contact inlet, which reduces the film thickness and could account for the slight divergence from a straight line in that range. In addition the film thickness quoted is the optical one:

$$\text{optical thickness} = \text{real thickness} \times \text{refractive index}$$

- The refractive index is not certain at these conditions since it increases with pressure and falls with temperature but, according to Paul and Cameron¹¹, probably changes less than 5%.

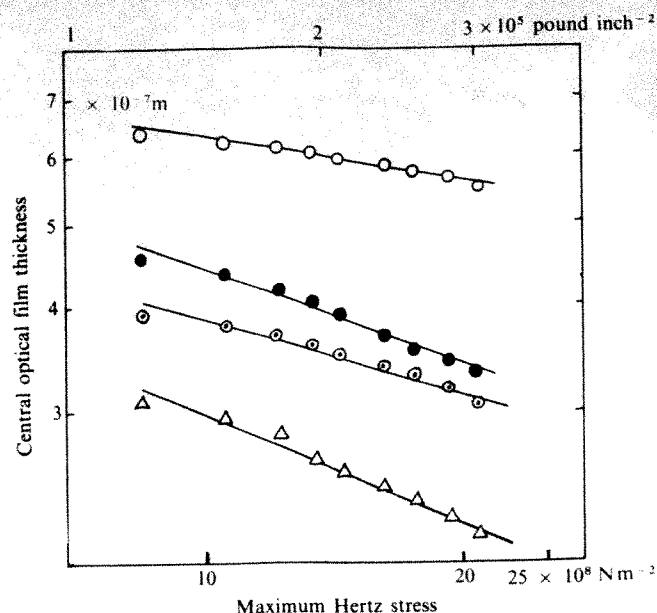


Fig. 2 Variation of film thickness with pressure. $\circ$, Fluid 1, 0.1 m s^{-1} , 28.5° C , $a=0.067$; $\circ$, fluid 1, 0.05 m s^{-1} , 28.5° C , $a=0.100$; $\triangle$, fluid 2, 0.1 m s^{-1} , 22° C , $a=0.144$; $\bullet$, fluid 3, 0.1 m s^{-1} , 22° C , $a=0.125$. Dowson and Higginson (line contact), $a=0.13$; Archard (point contact), $a=0.083$.

In conclusion it may be said that there was no evidence of a marked fall in film thickness for the three fluids beyond what it normally expected. It is difficult to compare against theory since various parameters, such as the pressure-viscosity coefficient, are not known, but there is certainly not the order of magnitude divergence found in ref. 10. There is therefore apparently a large discrepancy between optical measurements and X-ray measurements, even noting the difference in temperature range, film thickness and shear rate and that the former are central film thicknesses whereas the latter are minimum film thicknesses. Certainly film thickness data at these extreme pressures must be regarded with suspicion until a definitive study can be made of the problem.

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Speed of Sound in Bent Tubes and the Design of Wind Instruments

TRUMPETS, bassoons and other long wind instruments are made with bends for compactness. They would function best if each bend behaved acoustically just like a definable segment of straight tube. The custom of the craft is to make each bend a semi-torus of the same bore diameter as the straight tubes that it joins if these are cylindrical, and roughly a semi-torus of bore diameter intermediate between the diameters of the two straight tubes that it joins if these taper. This custom (which is very old) seems to find justification in the argument of Rayleigh¹ who, from the assumption that the velocity potential is always invariant over any section perpendicular to the bore, derived an equation according to which a curved tube is acoustically equivalent to a straight tube of the same cross-sectional area and the same length measured along the central axis. Nederveen³, by assuming the pressure to be always invariant over any cross-section of the bore and calculating the inertial consequences of his assumption without regard for continuity of the air, obtained the different result that a toric segment of bore diameter d , generator circle diameter D and length s measured along the central axis is acoustically equivalent to a cylinder of bore diameter $d\sqrt{a}$ and length s/a , where

$$a = (D\sqrt{2}/d) [1 - (1 - d^2/D^2)^{1/2}]^{1/2}$$

from his equations (37.6) and (37.9).

Now neither Rayleigh's nor Nederveen's assumptions can be quite true. Both imply strictly laminar flow; Rayleigh's directly because if the velocity potential is invariant over a plane there can be no component of velocity in that plane; and Nederveen's indirectly, because if the pressure is invariant over a plane there can be no component of acceleration in that plane. But strictly laminar oscillations in a torus are self-contradictory if inertia and continuity are both taken into account, since the lengths of inside and outside laminae are different. An exact theory seems likely to be very difficult. I therefore experimented with resonators. Each of these (Fig. 1) consisted of two straight tubes of lengths 36 and 72 cm and internal diameter 0.95 cm joined by a semi-torus of bore diameter 0.95 cm (later also smaller bore diameters) and generator circle diameter 1.3 or 4.5 cm. The resonators, with one end closed, were driven from an oscillator and loudspeaker so that there were 3, 9 or 15 quarter wavelengths from end to end. In each such mode of resonance, if the short end is closed the bend lies at a velocity antinode and if the long end is closed it lies at a velocity node. Table 1 shows the resonant frequencies (means and standard errors of means of three measurements).

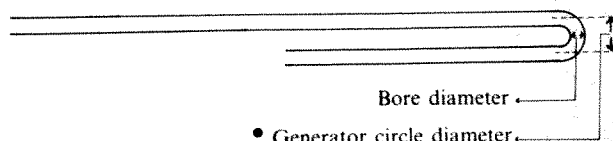


Fig. 1 One of the resonators used in the measurements (not to scale).

For each resonator and mode of resonance, measurements with the short end closed and with the long end closed were alternated. Thus any slow drifts in temperature which may have occurred are unimportant in this comparison. No such precautions were taken between measurements for different modes of resonance; it would therefore be unsound to use Tables 1 and 2 to calculate the effect of frequency on end-corrections.

It can be seen that the semi-torus is equivalent to a shorter straight tube when it is antinodal than when it is nodal. The effective shortening is roughly independent of frequency over

Table 1 Resonant Frequencies (Hz) of Resonators whose Toric Segments had Bore Diameter 0.95 cm and Generator Circle Diameters 1.3 cm or 4.5 cm

Mode of resonance	Generator circle diameter 1.3 cm		Generator circle diameter 4.5 cm	
	Long end closed	Short end closed	Long end closed	Short end closed
Quarter wavelength = 1/3 of tube length	227.8 ± 0.20	229.3 ± 0.13, difference = +1.5	223.9 ± 0.10	224.4 ± 0.13, difference = +0.5
Quarter wavelength = 1/9 of tube length	686.8 ± 0.25	691.1 ± 0.31, difference = +4.3	672.7 ± 0.06	673.9 ± 0.18, difference = +1.2
Quarter wavelength = 1/15 of tube length	1,150.0 ± 0.42	1,155.7 ± 0.32, difference = +4.8	1,128.8 ± 0.24	1,130.6 ± 0.30, difference = +1.8

the range investigated, the slight apparent decrease at high frequencies being probably mainly due to the fact that the torus then occupies an appreciable fraction of a wavelength. It is less for a gentler bend. An intermediate generator circle diameter (not shown in Table 1) gave an intermediate result.

The observed effect is in the same direction as that implied by Nederveen's formula and greater by a factor which varies, for the six examples in Table 1, between 1.2 and 1.8.

In a wind instrument that has to sound high modes of resonance it is undesirable that either the damping or the effective length should depend on the relation of the wave-pattern to any bends that are inserted not for their acoustic virtue but merely for compactness. The damping is presumably generally greater when velocity antinodes occur at bends, where the flow cannot be regular, than when they all occur in straight tube, where it can. The present experiments showed that this influence on damping is small, and almost certainly negligible for musical purposes; the *Q* at resonance was, for the resonators of Tables 1 and 2 and for another whose toric segment had bore diameter 0.86 cm, always the same within 1%, whichever end of the resonator was closed. The effective length is, on the contrary, influenced by the relation of wave-pattern to bends enough for the influence to be musically important. It can be corrected by joining straight cylindrical tubes with a torus not of the same bore diameter but of slightly less. From the results in Table 1, the perturbation theory of pipes (following Rayleigh²) predicts that for the first of the two resonators a reduction in bore diameter of torus from 0.95 to 0.91 cm should compensate. Experimentally, such a resonator gave the results shown in Table 2 (means and standard errors of means of three measurements).

Table 2 Resonant Frequencies of a Resonator whose Toric Segment had Bore Diameter 0.91 cm and Generator Circle Diameter 1.3 cm

Mode of resonance	Long end closed	Short end closed	Difference
Quarter wavelength			
= 1/3 of tube length	228.2 ± 0.13	228.2 ± 0.06	0.0
= 1/9 of tube length	689.4 ± 0.00	689.4 ± 0.11	0.0
= 1/15 of tube length	1,155.7 ± 0.37	1,155.1 ± 0.37	-0.6
Quarter wavelength			
= 1/5 of tube length	381.5 ± 0.06	381.7 ± 0.18	+0.2
= 1/7 of tube length	535.4 ± 0.06	535.8 ± 0.19	+0.4
= 1/11 of tube length	843.1 ± 0.08	843.1 ± 0.29	0.0
= 1/13 of tube length	998.1 ± 0.05	998.3 ± 0.23	+0.2

The resonant frequencies for 3, 9 and 15 quarter wavelengths in the tube are unaffected, within experimental error, by whether there is a node or an antinode at the bend. The results for 5, 7, 11 and 13 quarter wavelengths in the tube show that when, by reducing its bore, the bend has been caused to behave like the same length of straight tube whether nodal or antinodal, the compensation holds at least roughly for regions that lie between nodes and antinodes.

From these results it seems likely that it would be advantageous in wind instruments to reduce the bore diameter slightly at bends. The amount of reduction required will have to be determined by resonance measurements in each case unless an adequate theory of oscillatory flow round bends can be de-

veloped. The present observations suggest that for the rather tight bends of the butt of a bassoon or the valve slides of a trumpet it will be of the order of 5%.

The "speed of sound" in the ordinary sense is the product of frequency and wavelength, and is the same for travelling waves as for standing waves. If distances are measured along the centre line of the tube, sound goes faster along a toric bend than along a straight tube by a factor which, for the first resonator of Table 1, is about 1.09.

The very accurate toric tubes were made by Mr W. F. Piper.

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BIOLOGICAL SCIENCES

Inhibitor of DNA Polymerase in Sera of Tumour-bearing Mice

We have previously reported the existence of several DNA polymerases in the murine myeloma line, MOPC-21 (refs 1 and 2). Two of these polymerases, which we refer to as R-1 and R-2, are capable of synthesising poly(dT) on a poly(rA)-oligo(dT)₁₂₋₁₈ template. In this report, we show that the R-1 polymerase shares immunological determinants with the 'reverse transcriptase' of the Rauscher murine leukaemia virus (MLV). In addition, we show that mice inoculated with the MOPC-21 myeloma tumour line or the Rauscher-virus-induced MCDV-12 tumour line contain a non-immunoglobulin factor in their sera which specifically inactivates the R-1 polymerase.

The R-1 and R-2 polymerases were isolated from homogenates of MOPC-21 myeloma tumour by stepwise salt elution chromatography from DEAE-cellulose. Further purification of these fractions was achieved by phosphocellulose chromatography, as previously described^{1,2}. Purified rabbit immunoglobulin directed against the DNA polymerase of the Rauscher murine leukaemia virus was the gift of Drs G. Todaro and E. Scolnick³. Table 1 demonstrates that the R-1 polymerase is inhibited by specific antibody prepared against the MLV polymerase, and that the R-2 polymerase is not affected. This indicates that the R-1 polymerase derived from this tumour line shares common or related immunological determinants with this viral DNA polymerase.

If syngeneic Balb/c mice are inoculated with 10^5 MOPC-21 myeloma cells or comparable numbers of the MCDV-12 tumour line, the serum of these mice contains a factor which inhibits the action of the R-1 polymerase. The time course of appearance of the inhibitory factor is shown in Fig. 1. The sera of syngeneic mice bearing these tumours exhibit a progressive increase in their ability to inhibit the R-1 polymerase. In contrast, the sera of the allogeneic CFW mice receiving tumour cells display only minimal inhibition of the R-1 polymerase, and this inhibition remains essentially level coincident with initial growth of the tumour inoculum and its subsequent rejection. Inoculation of syngeneic spleen cells or repeated administration of the Rauscher MLV does not give rise to the appearance of inhibitor in the sera of Balb/c mice. As Fig. 2a shows, sera from Balb/c mice bearing the MOPC-21 myeloma tumour were as effective as comparable sera from MCDV-

Table 1 Inhibition of the Myeloma R-1 Enzyme by Antibody Specific for MLV Polymerase

Experiment 1	C.p.m. $^3\text{H-TMP}$ incorporated
R-1 + IgG (anti-polymerase)	4,469 $\pm$ 174 (n=2)
R-1 + IgG (non-immune)	12,740 $\pm$ 636 (n=2)
R-1 Control	14,961 $\pm$ 106 (n=3)
R-2 + IgG (anti-polymerase)	7,240 $\pm$ 135 (n=4)
R-2 + IgG (non-immune)	7,366 $\pm$ 247 (n=4)
R-2 Control	8,372 $\pm$ 756 (n=3)
Experiment 2	
R-1 + IgG (anti-polymerase)	11,127 $\pm$ 82 (n=3)
R-1 + IgG (non-immune)	15,936 $\pm$ 174 (n=3)
R-1 Control	16,124 $\pm$ 580 (n=2)
RMLV polymerase + IgG (anti-polymerase)	2,111 $\pm$ 56 (n=2)
RMLV polymerase + IgG (non-immune)	45,867 $\pm$ 975 (n=2)
RMLV Control	44,437 $\pm$ 843 (n=2)

Our standard assay for synthesis of poly(dT) by the R-1 polymerase or the Rauscher MLV polymerase using poly(rA)-oligo(dT)₁₂₋₁₈ as template was carried out in a volume of 250 μl . The reaction mixture contained 0.05 M Tris, pH 7.8, 4 mM β -mercaptoethanol (BME), 0.2 mM Mn^{2+} , 200 $\mu\text{g ml}^{-1}$ bovine serum albumin (BSA); $^3\text{H-TTP}$ was supplied at a specific activity of 4,839 c.p.m. pmol^{-1} , and each assay contained 1.08 nmol of TTP and 8.3 nmol of dATP. 0.05 A_{260} units of poly(rA)-oligo(dT)₁₂₋₁₈ was present as template, and the desired amount of enzyme was added to the reaction mixture in 50 μl . Incubation was carried out routinely for 60 min, at which time excess pyrophosphate, 200 μg yeast RNA and trichloroacetic acid were added and the reaction mixture was filtered through a Schleicher and Schuell B-6 membrane filter. The filters were dried and counted in a 0.02 POPOP-0.5% PPO-toluene scintillation mixture. Conditions for assay of the R-2 polymerase were similar except that Mn^{2+} was supplied at 1 mM. All assays were performed in duplicate. In experiment 1, 80 μg of purified rabbit immunoglobulin directed against the MLV polymerase was diluted to 35 μl in enzyme dilution buffer (0.02 M Tris-HCl, pH 7.8; 4 mM BME; 1 mg ml^{-1} BSA and 20% glycerol). A 5 μl sample of this mixture was added separately to 0.83 μg of the myeloma R-1 enzyme and to 0.94 μg of the myeloma R-2 enzyme, each in a total volume of 10 μl , and this mixture was held at room temperature for 30 min. At that time, 40 μl of enzyme dilution buffer was added along with 0.200 ml of assay buffer containing all of the components of our standard assay mixture employing poly(rA)-oligo(dT)₁₂₋₁₈ as template. In experiment 2, 40 μg of anti-polymerase IgG was diluted to 20 μl and 5 μl of this mixture was added separately to 0.83 μg of myeloma R-1 polymerase and to 6.0 μg of the Rauscher MLV polymerase (prepared according to the method of Ross *et al.*⁶) in a total volume of 15 μl . After 30 min at room temperature, 35 μl of dilution buffer was added along with 0.200 ml of assay buffer containing the rest of the reaction components. All incubations were carried out for 60 min at 37° C. As indicated, IgG prepared from a rabbit not exposed to the viral polymerase was run in parallel using 2.4 times the weight of IgG used in the anti-polymerase case. Reaction mixtures containing dilution buffer in place of IgG were also run as controls in parallel. The results are presented as the mean value of the number of observations indicated $\pm$ the standard error of the mean.

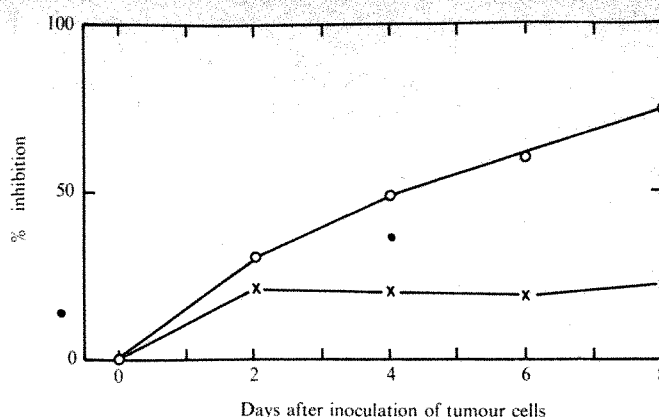


Fig. 1 Time course of development of polymerase inhibitor in serum. Balb/c (○) and CFW (×) mice were inoculated with 10^5 MCDV-12 tumour cells. Aliquots of serum were drawn on the days indicated and 1/8 dilutions prepared in enzyme dilution buffer. A sample of 75 μl of the respective dilutions was added to 8.1 μg of the R-1 polymerase in a total volume of 150 μl . These mixtures were left for 30 min at room temperature at which time 50 μl each of the mixtures was transferred to duplicate assay tubes and incubation continued for another 60 min at 37° C. The specific activity of the $^3\text{H-TTP}$ used in these assay mixtures was 4,570 c.p.m. pmol^{-1} . Under these conditions, this amount of enzyme catalysed the incorporation of 11.4 $\text{pmol } ^3\text{H-TMP h}^{-1}$.

12-bearing hosts in suppressing the activity of the R-1 polymerase. The inhibitor is not present in serum derived from normal mice.

Fractionation of serum from mice bearing the MCDV-12 tumour led to recovery of the inhibitor in the fraction of serum which was soluble in 50% ammonium sulphate solution. This fraction can be shown to be free of detectable immunoglobulin, and this is direct evidence that the inhibitor is not an antibody. Moreover, the inhibitor displays no nuclease activity against either the template or the product of the R-1 polymerase reaction (our unpublished observations). The striking specificity of the inhibitor on the action of the R-1 polymerase is shown in Fig. 2b. The inhibitor had no effect on the ability of polymerases derived from the avian myeloblastosis virus or the Rauscher MLV to synthesise poly(dT) using poly(rA)-oligo(dT)₁₂₋₁₈ as template.

As little inhibitor was found in the serum of mice in which these tumours were able to grow only briefly, we reasoned that the inhibitor was produced by the tumour and was not derived from the host animal. When allogeneic CFW mice were irradiated so as to depress their immune response to the point where they could no longer reject an inoculum of MCDV-12 tumour cells, substantial amounts of the R-1 polymerase inhibitor were detected in the sera of these irradiated mice after inoculation with the MCDV-12 tumour. This result strongly suggests that the R-1 inhibitor is produced by the tumour cell itself, and that the amount of inhibitor present in the sera of mice bearing the MCDV-12 tumour is proportional to the extent of growth of the tumour in a particular host. This conclusion is supported by the observation that irradiation of the MCDV-12 tumour cells themselves, before inoculation into syngeneic Balb/c mice, prevents the growth of that tumour in these mice, and no inhibition of R-1 polymerase activity is displayed by their sera (Table 2).

It is interesting that although the MCDV-12 tumour was originally induced by the Rauscher MLV, and produces a virus of high virulence, the myeloma line was initially induced with mineral oil and, while the MOPC-21 line contains type C particles resembling the Rauscher MLV, these particles are not particularly efficient at transforming other cells⁴. Nevertheless, both of these tumours produce

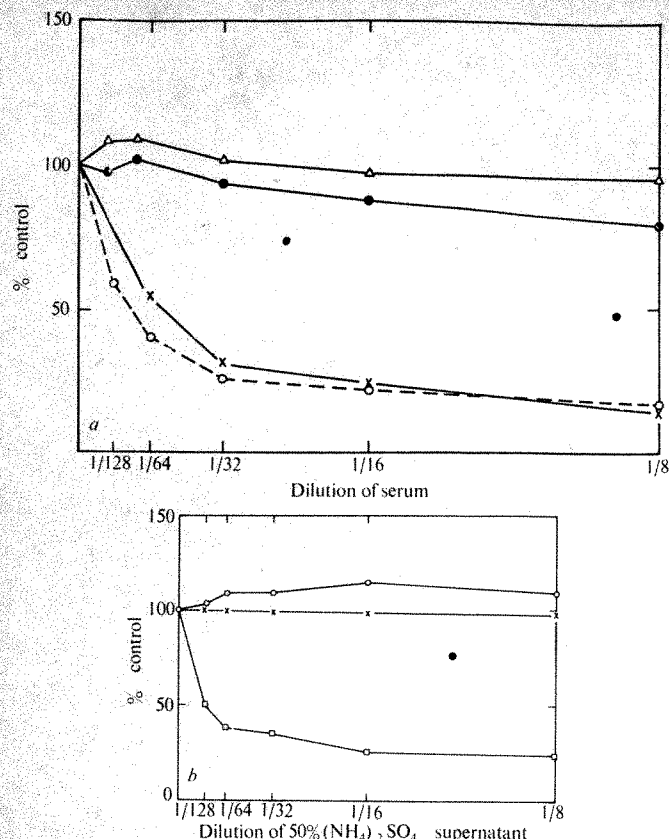


Fig. 2 Specificity of the R-1 inhibitor. *a*, Aliquots of sera from Balb/c mice bearing the MCDV-12 (x) or the MOPC-21 (O) tumour were drawn 7 d after inoculation and diluted as indicated in enzyme dilution buffer. 75 μ l of the respective dilutions of these sera was mixed with 75 μ l of a standard dilution of the R-1 polymerase (165 μ g ml⁻¹), and 50 μ l aliquots of these mixtures were treated as described in Fig. 1. In this study, the amount of enzyme used led to the incorporation of 4.6 pmol of ³H-TMP in the absence of serum. Sera from normal non-tumour-bearing Balb/c mice (Δ) and from CFW mice that received 10⁵ MCDV-12 cells (●) were assayed in parallel. *b*, Sera were collected from Balb/c mice inoculated 7 d previously with 10⁵ MCDV-12 cells. The supernatant fraction soluble in half-saturated (NH₄)₂SO₄ was prepared, and diluted as indicated in enzyme dilution buffer. 75 μ l of these dilutions was added to 75 μ l of enzyme dilution buffer containing 6.2 μ g of the R-1 polymerase ($\square$), or 9.0 μ g of the avian myeloblastosis virus polymerase (x), prepared according to the method of Kacian *et al.*⁷ or the Rauscher MLV polymerase (O). Incubation and assay were carried out as indicated in the legend to Table 1 except that 6 mM Mg²⁺ was substituted for Mn²⁺ in the assays utilising AMV. Under these conditions, in which the specific activity of the ³H-TMP used was 4,570 c.p.m. pmol⁻¹, the amounts of R-1, AMV and MLV polymerases in these assays catalysed the incorporation of 4.78, 7.98 and 4.28 pmol of ³H-TMP respectively. The protein concentration of the half-saturated ammonium sulphate supernatant was 9.8 mg ml⁻¹, as determined by the procedure of Lowry *et al.*⁸

an inhibitor which is specifically directed against a virus-related polymerase (R-1), and has no effect against other DNA polymerases, including the 'reverse transcriptase' of the Rauscher MLV. In these studies, the appearance of the R-1 inhibitor in serum seems to be correlated with tumour growth. At present, it is not known whether this inhibitor is unique to tumour cells or might, for example, be produced by normal cells which are growing rapidly. Moreover, the fact that such an inhibitor inactivates a cytoplasmic polymerase which is immunologically related to the DNA polymerase from Rauscher MLV, but has no effect on the viral polymerase itself, points out the necessity for caution in studies which attempt to distinguish between cellular and viral polymerases present in tumour cells.

It is particularly important to reinforce the distinction between immunoglobulin directed against a viral DNA

Table 2 Effect of Irradiation of Cells and Recipient Mice on Appearance of R-1 Polymerase Inhibitor in Serum

Serum from mice	C.p.m. ³ H-TMP incorporated	% Control
Experiment 1 (CF1 mice)		
Irradiated and given MCDV-12 cells	9,128	19.8
MCDV-12 cells alone, no radiation	33,986	73.8
Irradiated and given SRBC	44,540	96.8
SRBC alone, no radiation	44,856	97.5
Prior to being irradiated	49,162	106.8
Enzyme control (no serum)	46,027	100.0
Experiment 2 (Balb/c mice)		
Given irradiated MCDV-12 tumour cells	32,038	81.7
Given unirradiated MCDV-12 tumour cells	16,155	41.2
Normal, no treatment	34,730	80.9
Enzyme control (no serum)	39,212	100.0

In experiment 1, CF1 mice were irradiated with 700 r. before receiving 10⁵ MCDV-12 tumour cells of 1 $\times$ 10⁸ sheep red blood cells (SRBC). An equal number of mice was not irradiated and was challenged with MCDV-12 tumour cells and (or) SRBC. Serum was collected 7 d after challenge and pooled separately from both sets of mice and 75 μ l aliquots of a (1/8) dilution of these sera were mixed with 10.7 μ g of the R-1 polymerase in a total volume of 150 μ l, and held at room temperature for 30 min. Aliquots of 50 μ l of these mixtures were assayed in our standard assay system. Samples of sera drawn before irradiation were tested in parallel. In experiment 2, six Balb/c mice were inoculated with 7.5 $\times$ 10⁷ MCDV-12 cells which had been previously irradiated with 1,000 r. A separate set of six mice was given 10⁵ unirradiated MCDV-12 cells. Sera were obtained after 7 d, diluted 1/8 with enzyme dilution buffer, and mixed with 10.7 μ g of R-1 polymerase for 30 min at room temperature. Aliquots of 50 μ l were then removed and tested for residual polymerase activity. Sera from normal Balb/c mice were pooled and assayed in parallel.

polymerase and non-immunoglobulin inhibitory factors such as the one described herein which can selectively inactivate specific DNA polymerases.

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Use of ^{125}I in Fingerprinting RNA

It is often difficult to obtain highly radioactive *in vivo* ^{32}P -labelled RNAs from higher organisms for fingerprinting¹. In such situations, *in vitro* labelling methods can make a valuable contribution. One method using polynucleotide phosphokinase to introduce ^{32}P at the 5' terminus of oligonucleotides has been reported^{2,3}. Here I describe another method which is based on the fact that iodine has a high

slower in the second relative to unmodified oligonucleotides (Fig. 1a), indicating a greater net negative charge on them in agreement with the observed mobility of iodinated cytidylic acid⁷.

The results demonstrate the usefulness of ^{125}I for fingerprinting RNAs. The method is especially attractive because of its specificity, simplicity, speed and sensitivity. The fact that a fingerprint of a 'cold' RNA can be easily obtained by this method makes it a very useful procedure for studying

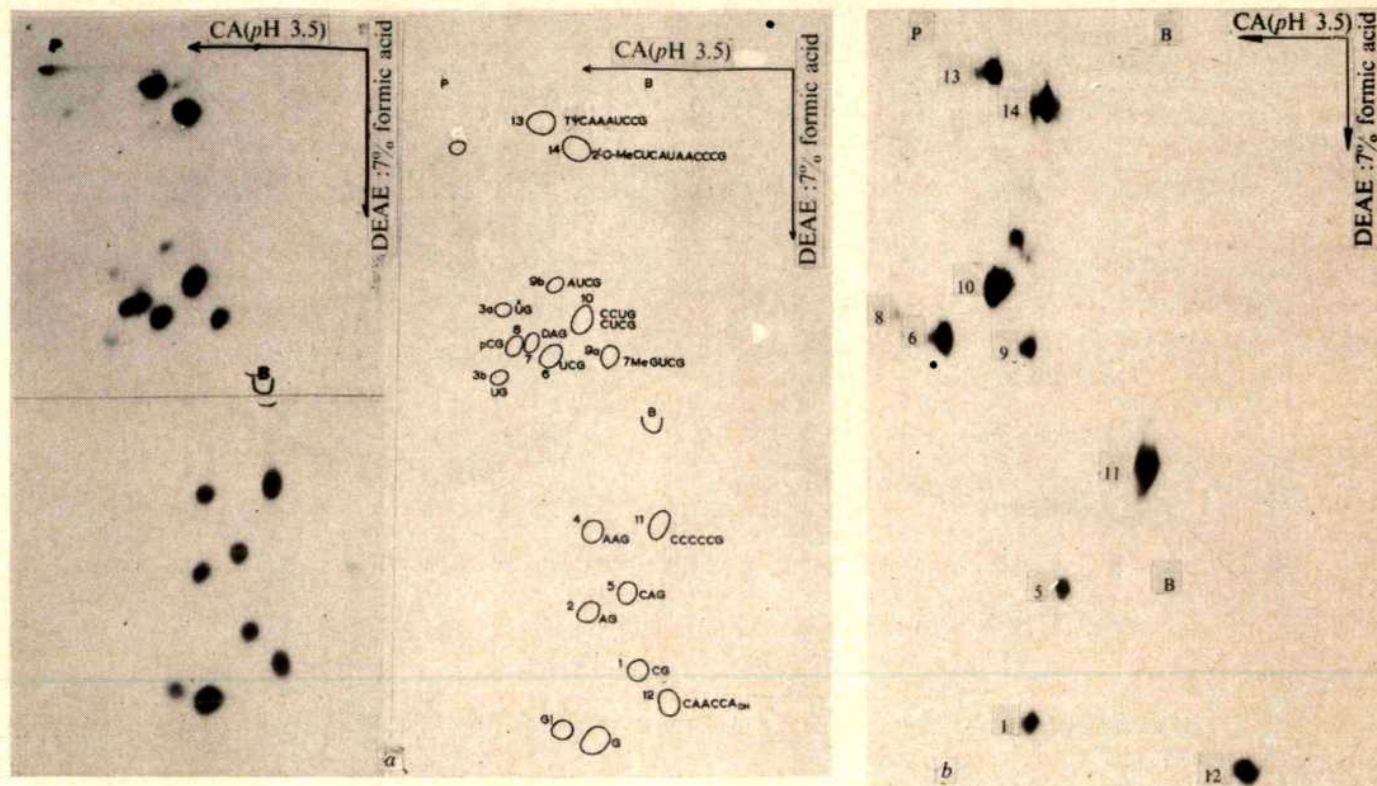


Fig. 1 A two-dimensional fractionation of an RNase T_1 digest of *in vivo* ^{32}P -labelled, (a), and *in vitro* ^{125}I -labelled, (b), *E. coli* tRNA^{Met}. tRNA^{Met} was prepared as described⁸. The tRNA was labelled with ^{125}I in a total volume of 2 μl containing 0.2 μg tRNA, 10 mM sodium acetate acetic acid buffer, pH 5.0, 0.01 mM KI equilibrated with 10 to 100 μCi Na^{125}I (Amersham, England) and 0.1 mM TiCl_3 (Merck, Germany). The reaction mixture assembled at 0°C , with reagents added in the above order, was taken up in a siliconised capillary tube which was afterwards sealed at both ends and incubated at 80°C for 10 min. The capillary tube was cooled on ice and broken open. Sodium thiosulphate (final concentration 1 mM) was added to reduce excess iodine and TiCl_3 . Then 20 μg carrier RNA (*E. coli* mixed tRNA) and ammonium acetate ammonia buffer, pH 9 (final concentration 0.2 M), was added. The capillary tube was sealed again at both ends and heated at 45°C for 2 h to convert the unstable 5-iodo-6-hydroxy-5,6-dihydropyrimidines back to the unsaturated form. After this the RNA was passed over a Sephadex G-25 column made out of a siliconised capillary tube. The fraction eluting at the void volume was precipitated with ethanol. The tRNA was digested with RNase T_1 with an enzyme to substrate ratio of 1 : 20 for 30 min at 37°C . The digest was fractionated on a two-dimensional high voltage electrophoretic system¹ using cellulose acetate, pH 3.5, for the first dimension and DEAE:7% formic acid for the second. The electrophoretogram was autoradiographed using Kodak X-Omatic H Film. The autoradiograph of the ^{125}I -labelled tRNA was obtained by exposure of the film for 8 to 12 h. The diagram shows the positions of the oligonucleotides (a) with their identification numbers and sequences⁸. B is the blue marker; P is the dye marker peak.

specificity for cytosine under certain conditions⁴ and that iodine isotopes (^{125}I , ^{131}I) are easily detectable by autoradiography. I have used *Escherichia coli* formyl-methionine tRNA of known sequence^{5,6} to test the suitability of this method for fingerprinting RNAs. The results show that a fingerprint of pmol amounts of RNA is obtainable within 2 d.

Figure 1b shows an RNase T_1 fingerprint of iodinated tRNA^{Met} and Fig. 1a that of the *in vivo* ^{32}P -labelled tRNA^{Met}. The accompanying diagram gives the nucleotide sequences of the oligonucleotides. Several points in the figure are noteworthy. The fingerprint of iodinated tRNA is identifiable with that of the ^{32}P -labelled tRNA. Only cytosine containing oligonucleotides are prominent on the fingerprint and their intensity is in good agreement with their cytosine content, indicating that, in the conditions used for labelling, the secondary structure of RNA is sufficiently opened up to make possible uniform iodination. The iodinated oligonucleotides move slightly faster in the first dimension and

homologies between closely related RNAs from different species, cell types and RNA tumour viruses.

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Repair Endonuclease-sensitive Sites in Daughter DNA of Ultraviolet-irradiated Human Cells

WE have used cells that were derived from individuals with xeroderma pigmentosum (XP) and are defective in excision repair¹ to demonstrate the appearance of ultraviolet lesions in the DNA made after ultraviolet irradiation. Normal human and XP cells were irradiated and labelled with either ³H-thymidine or ³²P₄ for 6–8 h, the label was removed, and the cells were further incubated for 18 h to allow for DNA chain elongation and joining of the short DNA segments synthesised after irradiation. The cells were then osmotically shocked, treated with a repair endonuclease contained in *Micrococcus luteus* extract for 5 min at 37° C and pH 8.0, and sedimented in 5–20% alkaline sucrose gradients. The enzymatic assay² and the sedimentation procedure³ have been described elsewhere. Figure 1 shows that daughter DNA from irradiated and non-irradiated normal human cells contains no repair endonuclease-sensitive sites. This is expected because normal human cells excise and repair most of the pyrimidine dimers formed after ultraviolet irradiation⁴. Figure 2 shows that DNA synthesised by irradiated XP cells does contain repair endonuclease-sensitive sites, although the number appears to be small. Under our experimental conditions there is approximately one sensitive site for every fifteen to thirty-five dimers in the parental DNA⁵.

The repair endonuclease-sensitive sites could result from (a) DNA exchanges between parental and daughter strands, (b) insertion of abnormal bases into the DNA made from irradiated templates and the recognition of these abnormal bases by the repair endonuclease, or (c) recognition of the dimer but incision into the DNA strand not containing the dimer.

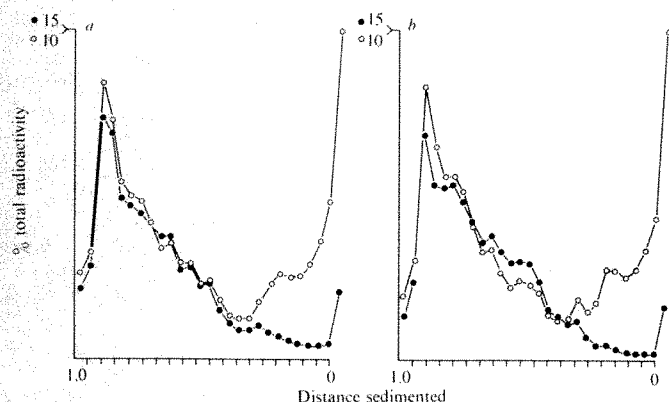


Fig. 1 Alkaline sucrose gradient profiles of DNA from cells of normal human cell line HSWP which were ultraviolet-irradiated with 150 erg mm⁻² (●) or non-irradiated (○) incubated in 12.5 μCi ml⁻¹ of ³H-thymidine (specific activity 18.1 Ci mmol⁻¹) or 30 μCi ml⁻¹ of ³²P₄, respectively, for 8 h. The label was removed and the cells were incubated for 18 h before (a) sedimentation or (b) treatment with repair endonuclease extract from *M. luteus* and sedimentation. Sedimentation was for 180 min at 25,000 r.p.m. in a 2 M salt–5–20% alkaline sucrose gradient. The ³H and ³²P profiles in both (a) and (b) were co-sedimented. Total c.p.m. (a, ●) 3,897; (a, ○) 14,832; (b, ●) 2,612; (b, ○) 11,631.

DNA exchanges between parental and daughter strands have been observed in irradiated *Escherichia coli* cells analysed in CsCl density gradients⁶, and repair endonuclease-sensitive sites have also been observed in the daughter DNA of irradiated *E. coli* cells (A. Ganesan, unpublished observations). However, attempts to demonstrate DNA exchanges between parental and daughter strands in mitotic cells (ref. 7 and S. N. B. and J. D. R., unpublished observations) or somatic recombination (ref. 8 and G. Pontecorvo, personal communication) in mammalian cells have been unsuccessful.

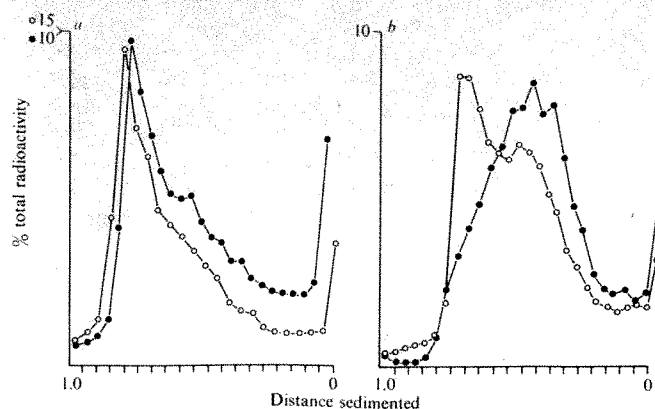


Fig. 2 Alkaline sucrose gradient profiles of DNA from cells of XP cell line SG-XP4 which were ultraviolet-irradiated with 150 erg mm⁻² (●) or non-irradiated (○) and incubated in 25 μCi ml⁻¹ of ³H-thymidine (specific activity 18.1 Ci mmol⁻¹) for 8 h. The label was removed and the cells were incubated for 18 h before (a) sedimentation or (b) treatment with repair endonuclease from *M. luteus* extract and sedimentation. Sedimentation was for 150 min at 25,000 r.p.m. in a 2 M salt–5–20% alkaline sucrose gradient. Each profile was individually sedimented. Total c.p.m. (a, ●) 6,489; (a, ○) 8,312; (b, ●) 5,440; (b, ○) 3,300.

cells DNA synthesised from ultraviolet-irradiated templates contains discontinuities⁹, and that ~75% of the discontinuities are completed by insertion of exogenous nucleotides¹⁰. During completion of the discontinuities, abnormal bases could be inserted, and the resulting structural abnormalities could be recognised by endonucleases in the *M. luteus* extract, so that incisions would be made in the DNA. The insertion of such abnormal bases could lead to accumulation of errors in the DNA and result in the XP phenotype, which is characterised by the appearance of skin cancers at a very early age¹¹. Although previous results show that the repair endonuclease is specific for the strand containing the dimer^{12,13}, minor non-specificity results in one incision in the strand not containing the dimer for every seventy dimers in the complementary strand¹³.

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Differences in Murine Leukaemia Virus-specific DNA Sequences in Normal and Malignant Cells

In many mouse strains, RNA tumour virus information is transmitted vertically (inherited) perhaps as part of the cell genome^{1,2}. The activation of type C virus replication in cells from low leukaemia incidence mouse strains³ and from 'virus-free' cell lines⁴ by halogenated pyrimidines suggests that all mouse cells may contain murine leukaemia virus (MuLV) information, often in an unexpressed form. Indeed, proponents of the 'oncogene' hypothesis have predicted a complete copy of type C virus information in the genome of all somatic cells⁵.

Varmus *et al.*⁵, using acceleration of reannealing kinetics of radioisotopically labelled double stranded DNA product from a reverse transcriptase reaction, by unlabelled cell DNA, have shown that the amount of virus information was the same in the DNA of cells from low and high mammary tumour (MMT) incidence strains. Using similar techniques, Gelb *et al.*⁶ failed to demonstrate a difference in viral DNA content of normal and virus-transformed cells. Similar results have been obtained using an avian oncornavirus system⁷. Thus, if RNA tumour virus information is similar in mouse strains with different tumour frequencies and in normal and transformed cells, oncogenesis would depend on factors in addition to virus structural genes (for example, regulatory genes, biological or chemical agents or ageing).

In an attempt to further characterise leukaemia virus DNA content in mouse cells we have synthesised *in vitro* a radioactively labelled single stranded DNA copy of the naturally occurring AKR (Gross) murine leukaemia virus (AKR-V) and the Rauscher leukaemia virus (RLV). These probes were used in DNA-DNA hybridisation and saturation experiments with DNA from normal cells of low and high leukaemia incidence mouse strains and virus-induced lymphomas. Our results indicate quantitative and qualitative differences among the various cellular DNA preparations as demonstrated by extent of hybridisation, reannealing kinetics and thermal stability of the various DNA duplex hybridisation products.

Viral ³H-DNA was synthesised by an endogenous reverse transcriptase reaction in the presence of actinomycin D, in order to inhibit viral and host DNA-directed DNA synthesis. The viral probe was purified by utilising phenol-cresol, alkali hydrolysis of RNA, and Sephadex and hydroxyapatite chromatography⁸. The probes were self-annealed⁹ and less than 0.5% was found to be double stranded. Both viral ³H-DNA probes had a sedimentation coefficient of 5–8S in an alkaline sucrose equilibrium gradient. They hybridised completely to purified viral RNA and not to synthetic polyribonucleic acid. The latter hybridisation was done specifically to rule out the possibility of transcription from polyadenylic acid regions of the viral genome¹⁰. Cell DNA was extracted from a high incidence mouse strain (AKR) and low incidence strains (Balb/c, NIH Swiss) and Rauscher and Gross virus-induced lymphomas by the method of Britten *et al.*¹¹ using batch elution from hydroxyapatite powder followed by mechanical shearing to a piece size comparable with the viral ³H-DNA. All cell DNA reannealed completely after denaturation. Hybridisation experiments were carried out to a C_0t value of 3,000, which represented the terminal plateau of the reannealing curve (see below). C_0t equals starting DNA concentration $\times$ time (mole $\times$ s l⁻¹), as defined by Britten and Kohne¹².

Table 1 shows more extensive hybridisation of AKR-³H-DNA than RLV-³H-DNA with all of the mouse DNA preparations tested. The percentage of the AKR probe hybridised was greatest with lymphoma DNA and success-

sively less than normal AKR, Balb/c and NIH Swiss DNA. In hybridisation experiments using RLV-³H-DNA, we were unable to demonstrate differences in mouse strains. There was, however, more extensive hybridisation of the RLV probe to lymphoma than to normal DNA. Reannealing curves, which also reflect the concentration of complementary sequences in the cell DNA, demonstrated more rapid reannealing of the AKR probe with lymphoma and normal AKR DNA than with NIH Swiss DNA (Fig. 1). A plateau is reached at a C_0t value of approximately 3,000, after which no further hybridisation of the AKR-³H-DNA with any of the cell DNA preparations could be detected.

Table 1 Hybridisation of Virus-directed ³H-DNA with Cellular DNA

	AKR- ³ H-DNA			RLV- ³ H-DNA		
	% Hybridised	$T_m^{(e)}$	(°C)	% Hybridised	$T_m^{(e)}$	(°C)
	60° C	80° C		60° C	80° C	
Normal mouse DNA						
AKR	50.1	23.5	79.5	22.2	7.5	75.5
Balb/c	40.0	13.6	77.5	22.5	5.1	73.0
NIH Swiss	35.5	8.3	75.0	20.1	7.6	74.0
Lymphoma DNA						
Gross	54.6	27.7	80.5	35.6	12.6	78.0
Rauscher	59.9	25.8	78.5	48.9	20.2	77.5
Salmon sperm DNA	1.0	0	<65	2.4	0	<65

Hybridisation of viral ³H-DNA probes with cell DNA. RLV was obtained from the plasma of infected mice²¹; AKR-V was obtained from Electronucleonics Corp. Virus (250 µg protein) in 150 µl Tris (hydroxymethyl aminomethane), pH 8.3, was ruptured by incubating for 10 min at 4° C in the presence of 0.003% Nonidet P-40 (Shell) and 30 mmol dithiothreitol. The virus sample was made to a volume of 375 µl with an incubation mixture containing: 19.2 mmol Tris, pH 8.3, 18 mmol KCl, 3.1 mmol MgCl₂, 0.2 µmol dATP, dCTP, and dGTP, and 0.6 mCi ³H-TTP (specific activity 24,000 c.p.m. pmol⁻¹), and 37 µg actinomycin D, and incubated for 45 min at 37° C. The reaction was terminated by addition of NaCl and sodium dodecyl sulphate (SDS) to a final concentration of 0.4 M and 1%, respectively. An equal volume of phenol-cresol (7:1) containing 0.4 g 8-OH quinoline per 100 ml was added to the sample, mixed and centrifuged at 5,000g for 5 min at 25° C. The aqueous phase was removed and placed on a Sephadex column (G50, medium) with a total bed volume of 100 ml; 0.5 ml fractions were collected and fractions from the DNA region of the gradient were pooled. NaCl (to 0.4 M) and 10 µg ml⁻¹ carrier yeast RNA were added and the nucleic acid precipitated with 2 volumes of cold ethanol for 12 h at -20° C. The solution was centrifuged at 12,000 r.p.m. for 30 min at 4° C and the pellet resuspended in 100 µl 0.3 M NaOH and kept at 37° C for 18 h to hydrolyse RNA. The sample was neutralised with HCl and brought to 0.024 M in phosphate buffer (PB) containing equimolar parts of Na₂HPO₄ and NaH₂PO₄, pH 6.8. The sample was passed through a hydroxyapatite column (2 cm deep and 1 cm in diameter) at 60° C, and eluted with 0.4 M PB. The nucleic acid preparation obtained was self-annealed for 96 h at 60° C and double stranded DNA separated using a hydroxyapatite column²². Normal adult livers were used as a source of AKR, Balb/c and NIH Swiss DNA. Lymphomatous DNA was obtained from virus-induced tumours which were serially transplanted in low-leukaemia incidence strains (Gross lymphoma in C57/6 bl, Rauscher lymphoma in Balb/c). Salmon sperm DNA was purchased from Sigma. Whole cell DNA was extracted by the method of Britten *et al.*¹¹ which consists of homogenising tissue in the presence of urea, PB and sodium perchlorate, extraction with chloroform-octanol (24:1) and purification by hydroxyapatite chromatography. DNA fragments were prepared by mechanical shear (50,000 pounds per square inch) and passed through cellulose acetate filters. The ratios of A_{260} to A_{280} of the DNA preparations were all close to 2. Annealing reaction mixtures contained 6 A_{260} units of cell DNA, 0.5 pmol of ³H-DNA, 2% SDS, 10⁻³ EDTA in 500 µl PB adjusted to 0.5 M. The mixture was heated for 10 min at 100° C and placed in a 60° C water bath for 120 h ($C_0t = 3 \times 10^3$)⁹. The sample was then diluted to 0.14 M PB and passed over a hydroxyapatite column (2 cm in depth) previously equilibrated with 0.14 M PB containing 4% SDS at 60° C. The double stranded DNA was eluted with 0.4 M PB and radioactivity counted in a liquid scintillation counter using Instagel (PacRad) scintillation fluid. Thermal elutions were performed by loading the column with annealing mixtures diluted to 0.14 M PB and raising the temperature of the column by 5° C increments from 60° to 100° C and eluting with 2 ml 0.14 M PB and counting radioactivity as described above. The percentage hybridisation at 80° C refers to the fraction of the probe remaining double stranded (hybridised) when the column temperature was raised to 80° C.

The differences in extent of hybridisation and reannealing kinetics among the DNA preparations tested indicate quantitative differences in MuLV information in cell DNA. The thermal stability profiles (Fig. 2) of the hybrid DNA duplexes indicated that there are qualitative differences also. $T_{m(e)}$, derived from the thermal elution curves, represents the temperature at which 50% of the double stranded DNA is eluted from the hydroxyapatite column and correlates well with T_m obtained by optical methods¹². The $T_{m(e)}$ of hybrids formed with the AKR probe was higher than those formed with the RLV probe for all DNA samples tested. Haapala and Fischinger¹³ have reported considerable molecular divergence among the genomes of various mouse leukaemia viruses. The higher $T_{m(e)}$ obtained with AKR-³H-DNA hybrids possibly represents more precise base pair matching with the naturally occurring MuLV probe.

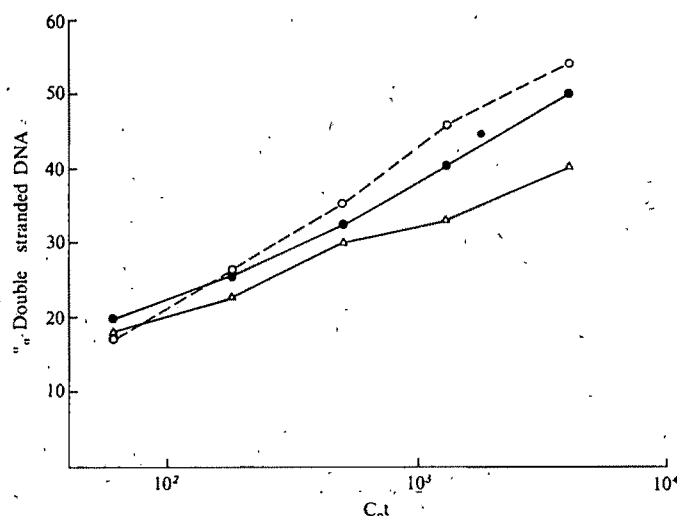


Fig. 1 Annealing curves of AKR-³H-DNA with Gross lymphoma (O), AKR (●), and Balb/c (▲) DNA. Each point represents a 100 μ l aliquot removed from a 0.5 ml reaction mixture incubating at 60° C. Double stranded DNA was determined by fractionation on hydroxyapatite as described previously.

The hybrids formed with AKR-³H-DNA, in order of decreasing $T_{m(e)}$, were Gross lymphoma>AKR>Rauscher lymphoma>Balb/c>NIH Swiss DNA. The thermal stability of polynucleotide duplexes depends on their length, base composition and relative composition of complementary base pairs. Since the piece sizes of cell DNAs were similar, the higher thermal stability of duplexes formed by AKR-³H-DNA with lymphoma and AKR DNA compared with Balb/c and NIH Swiss DNA indicates more precise base pairing and (or) the existence of additional base pairs with a high G:C content in the former DNA preparations.

Thus, one possibility is that there was a greater degree of molecular divergence (that is, mutation) of the MuLV nucleotide sequences in the low incidence mouse strain genome accounting for the lower $T_{m(e)}$ of the hybrid formed with the AKR probe.

Another possibility is that AKR and lymphoma DNA contain additional information not present in low leukaemia incidence mouse DNA; recycling experiments¹⁴ were performed to test this possibility. AKR-³H-DNA was extensively hybridised to NIH Swiss DNA. NIH Swiss DNA was present in great excess and the reaction was taken to a C_0t value of 10,000 at 60° C. This is a C_0t value where all complementary probe sequences are saturated with cell DNA and no additional hybridisation of the probe

will occur when incubated with NIH Swiss DNA. The non-hybridised fraction of the probe was separated using a hydroxyapatite column and incubated with AKR and Gross lymphoma DNA and 2.5% and 6.4% of the recycled probe hybridised, respectively. Thus, it seems that AKR probe sequences are present in normal AKR and lymphomatous DNA that are not present in NIH Swiss DNA.

A critical factor in experiments using ³H-DNA probes synthesised *in vitro* is the possibility of asymmetrical transcription with certain viral sequences being transcribed preferentially and others not at all⁶. This might account for the differences we observed between the two viral probes. Nevertheless, using probes synthesised in this manner, the AKR probe may offer certain advantages over the RLV probe. RLV-³H-DNA has previously been used extensively in detecting complementary MuLV sequences in other species^{8,15,16}.

These results contrast with previous reports demonstrating little difference in tumour virus DNA content in normal and neoplastic cells^{6,7} and in low and high tumour incidence strains^{5,17}. Gelb *et al.*¹⁷ were unable to find a difference in the number of MuLV genome equivalents in mouse embryo DNA from different strains using acceleration of reannealing kinetics of Kirsten leukaemia virus-specific double stranded DNA. In our experiments adult liver was used as a source of cellular DNA. AKR embryos are free of detectable MuLV; virus replication begins shortly after birth in certain cells, viraemia occurs and an exogenous viral infection probably occurs in liver cells¹⁸. This phenomenon could explain the quantitative differences we observed in MuLV-specific DNA in AKR and NIH Swiss DNA, but does not adequately explain the differences in $T_{m(e)}$ of hybridisation products and the results of recycling experiments we observed between these two strains.

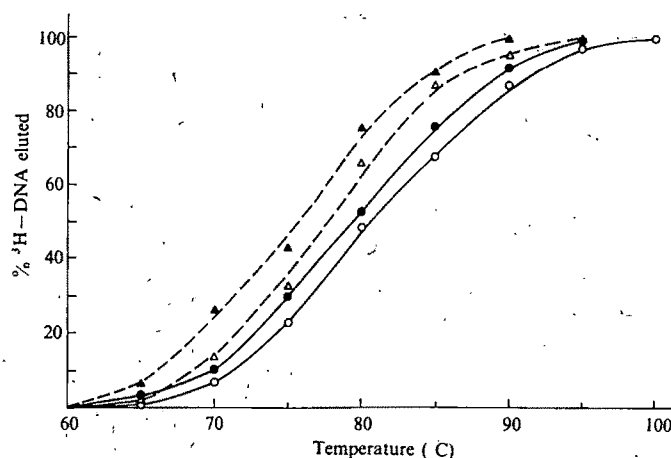


Fig. 2 Thermal stability curves of DNA duplex formed by AKR-³H-DNA probe and cell DNA hybridisation. The methods are described in the legend to Table 1. Cell DNAs are normal AKR (●), Balb/c (△), NIH Swiss (▲) and Gross lymphoma (○).

Balb/c and NIH Swiss cells contain sufficient information for MuLV replication^{2,3}. It has not been determined if the differences between AKR and the two low leukaemia incidence strains we have detected in these hybridisation experiments represent additional information essential for neoplastic transformation, which low incidence strains are lacking. There is no evidence so far that chemically induced type C viruses from low tumour incidence strains of any species are leukaemogenic^{19,20}. Therefore, it is possible that some mouse cells contain information for infectious type C viruses that are non-oncogenic.

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Biochemical Parameters correlated with Tumour Cell Implantation

FIDLER¹ has described melanoma cell lines produced by serial injection into and collection from C57 mice, some lines of which produce few pulmonary metastases while others have

greatly increased metastatic potential. These cells also grow in culture and retain their respective metastatic or non-metastatic character^{1,2}. These cell lines are particularly useful for studying metastasis since all cells are tumorigenic, and one is therefore not faced with making a choice of an appropriate 'normal' cell or tissue to act as a control with which to compare neoplastic or metastatic potential. Dr Fidler kindly supplied us with cell lines 26 (low metastasis) and 37 (high metastasis). Culture conditions and maintenance were as described¹. Since metastasis would seem intuitively to be intimately concerned with plasma membrane properties, we initiated extensive studies on cell surface properties of these cells. We report here the results of these studies and some findings relating to cell growth that may define the process of cell metastasis. It should be pointed out, however, that under the conditions defining the cell lines, implantation, more than metastasis, is being studied. Metastasis implies the ability of a cell to leave a given tumour site, be transported to another site, and implant and grow there; in the studies described here only the last two conditions of metastasis obtain and hence implantation properties are probably being studied.

First we injected 67,000 line 26 cells (in 0.2 ml of saline) into the tail vein of each of five C57 mice and 45,000 line 37 cells (in saline) into five C57 mice. The cells were over 95% viable and were counted on a Coulter Counter Research Model B. Controls received 0.2 ml of saline. Three weeks later, at killing, controls had 0, line 26 had 1.8 ± 0.1 , and line 37 had 11.4 ± 0.5 melanin-containing tumour foci in the lungs (significant at $P < 0.01$). Thus line 37 had produced more than five times as many tumour foci as had line 26, even though 50% more line 26 cells had been inoculated into each mouse.

At first we confined our work to cells that were just confluent (40×10^3 cells cm^{-2}) but found that in many of the experimental parameters related to cell surfaces there was little or no difference between line 26 and line 37 (see below). We therefore looked at sparse cultures so as to better characterise the system. Cell line 26 had a doubling time of 20 h and cell line 37 had a doubling time of 18 h; cell volumes were essentially the same as recorded by the Coulter Counter Volume Plotter. 'Confluent cells' are defined here as cells harvested when they begin to touch each other on the growth plate, a density of about 40×10^3 cells cm^{-2} . 'Sparse cells' are cells collected at a density of 0.8×10^3 cells cm^{-2} . Intermediate cell densities were also studied, and results were found to be essentially intermediate between results for sparse and confluent cultures and were related to cell culture density. Protein determinations³ and cell counts showed that, whether cultures were sparse or confluent, cell line 26 had $1.6 \pm 0.1 \times 10^{-6}$ mg of protein per cell, whereas line 37 had $1.2 \pm 0.1 \times 10^{-6}$ mg of protein per cell.

It soon became evident that the surface properties of the two cell lines were very different. This difference could be due to either one of two parameters: the absolute age of the cell when collected, or the age or state of the interaction

Table 1 Electrophoretic Mobilities of Cells

Condition	Electrophoretic mobility ($\mu\text{m}^{-1} \text{V}^{-1} \text{s}^{-1} \text{cm}$)			
	26 Sparse	37 Sparse	26 Confluent	37 Confluent
Control	-2.10 ± 0.04	-2.77 ± 0.06	-2.11 ± 0.03	-2.07 ± 0.04
Neuraminidase *	-1.95 ± 0.02	-2.11 ± 0.04	-1.92 ± 0.04	-1.90 ± 0.06
20 μg	-1.54 ± 0.04	-1.69 ± 0.11	-1.46 ± 0.07	-1.40 ± 0.10
50 μg	-1.09 ± 0.02	-1.10 ± 0.04	-1.08 ± 0.09	-1.05 ± 0.08
50 μg , boiled	-2.11 ± 0.05	-2.78 ± 0.07	-2.10 ± 0.04	-2.10 ± 0.06
Trypsin *, 50 μg	-2.19 ± 0.07	-2.89 ± 0.04	-2.26 ± 0.06	-2.20 ± 0.07
Hyaluronidase *, 50 μg	-2.04 ± 0.03	-2.64 ± 0.02	-2.01 ± 0.04	-2.00 ± 0.10

Values are means $\pm$ s.e.m. and are for cells measured in 0.0145 M NaCl, 4.5% sorbitol, 0.6 mM NaHCO_3 , pH 7.2 ± 0.1 at $25^\circ \text{C} \pm 0.1$, as previously described^{5,15}.

* Enzyme treatment given as amount per mg cell protein.

Table 2 Partitioning of Cells in Two-phase Aqueous Polymer System

Density	Partition ratios *	
	Cell line 26	Cell line 37
Sparse	0.361	0.432
Confluent	0.174	0.180

Cells were partitioned in a two-phase aqueous polymer system as described by Walter *et al.*^{7,8}. The system was composed of 5% (w/w) Dextran T500 (Pharmacia; Lot No. 1342), 3.5% (w/w) polyethylene glycol (Carbowax 6,000, Union Carbide), equimolar amounts of NaH_2PO_4 and Na_2HPO_4 (total concentration 0.10 M, pH 6.98), and 0.05 M NaCl. Cells were partitioned in 15 × 150 mm test tubes for 1 h at 5° C. Cell number was determined in aliquots of total system before partition and top phase after partition, using a Coulter Counter Model ZB with a 100 μm aperture and Isoton (Coulter) as electrolyte. Partition ratios were calculated as top phase cell number divided by total system cell number.

* Means of four observations each, consisting of ten independent partitions.

between the cell and its support (glass) at the time of collection. Our data suggest that the major surface property differences occur in sparse cultures and that implantation potential is manifest primarily during this time period, inasmuch as surface properties of confluent cells of the two lines seem to be similar.

Electrophoretic mobilities of the two cell lines under various conditions are shown in Table 1, as follows: (1) Sparse cells of line 37 had a much higher electrophoretic mobility than sparse cells of line 26, but confluent cells of both lines had essentially the same mobility. (2) Treatment of all cells with neuraminidase reduced their electrophoretic mobility, and when sparse 37 cells were treated with 50 μg of neuraminidase per mg of cell protein, their mobility was equivalent to that of 26 cells so treated. Measurement of released sialic acid⁴ showed that treatment with 50 μg of neuraminidase per mg of cell protein released 2.5 ± 0.1 μg of sialic acid per mg of cell protein from sparse 37 cells but only 1.0 ± 0.1 μg from sparse 26 cells or confluent 37 and confluent 26 cells. (3) Trypsin treatment and hyaluronidase treatment had little effect on cell mobilities in any of the lines tested; interpretation of similar data for other cell lines is given elsewhere⁵. Thus, when sparse, line 37 had a much higher electrophoretic mobility than sparse 26 cells, and 2.5 times as much neuraminidase-susceptible surface sialic acid.

A more sensitive parameter than whole-cell microelectrophoresis is partition of cells into two-polymer aqueous phase systems, whereby not only surface charge but also some other, poorly defined phenomena are measured⁶⁻⁸. Using

Table 3 Proteolytic, Glycosidase, and Acid Phosphatase Activities of Cells

Enzyme	Cell line 26 ($\mu\text{mol per h per } 10^6$ cells)	Cell line 37 ($\mu\text{mol per h per } 10^6$ cells)
β -D-galactosidase (EC 3.2.1.23)	14 ± 2	68 ± 14
β -L-fucosidase (EC 3.2.1.38)	119 ± 27	339 ± 49
N-acetyl- β -D-galactosaminidase (EC 3.2.1.—)	877 ± 121	$2,388 \pm 240$
N-acetyl- β -D-glucosaminidase (EC 3.2.1.30)	626 ± 78	$1,511 \pm 129$
α -D-mannosidase (EC 3.2.1.24)	175 ± 29	194 ± 48
Acid phosphatase (EC 3.2.3.2)	606 ± 121	610 ± 68
Proteolytic pH 3.4 (cathepsin-like)	28 ± 3.6	69 ± 8.9
Proteolytic pH 7.4 (trypsin-like) (EC 3.4.4.4)	1.2 ± 0.2	3.5 ± 0.2

Values are mean activity $\pm$ s.d. All data were determined for sparse cultures on 0.1% Triton X-100 homogenates of the cell lines^{9,16}. Proteolytic activity was determined using ³H-acetyl haemoglobin as substrate¹⁷. Glycosidase and acid phosphatase activity was determined using *p*-nitrophenyl derivatives as described^{9,16}.

this technique, we found that in sparse culture, line 37 had a much higher partition ratio than line 26 (Table 2), probably indicating, in part, a higher charge⁷. Confluent cells of the two lines had similar partition ratios, but these values were vastly different from the values for sparse cells of either line. Thus, as measured by this parameter, both cell lines show marked differences in cell surface properties between the sparse and confluent cell cultures.

One biochemical change considered in implantation or metastasis is increased levels of degradative enzymes, presumably to enhance the infiltrative capacity of the cell and perhaps for the phenomenon of sublethal autolysis^{9,10}. The data in Table 3 for sparse cultures indicate that line 37 had generally elevated levels of glycosidases and proteases (α -mannosidase and acid phosphatase levels were similar to those of line 26). Confluent cells of lines 26 and 37 had levels of activity similar to those of sparse line 26 (not shown in the table).

Table 4 compares the activity levels of glycoprotein: glycosyl transferases in cells of both lines, using endogenous or exogenous acceptors and based on a whole cell Triton X-100 homogenate. In the line 37 cells the activity levels of many of these transferases were elevated above the levels in the 26 cells. The highest elevations were in the sparse cultures, but elevations were clearly evident in the confluent 37 cells compared to the confluent 26 cells.

Table 4 Total Glycoprotein: Glycosyl Transferase Activities of Cell Lines

Transferase	Cell line			
	Sparse 26	37 (c.p.m. per 10^6 cells)	Confluent 26	37
Collagen: glycosyl *	7,870	27,750	10,460	20,700
Endogenous glucose	8,200	17,960	8,200	8,600
Fetuin: sialyl †	11,320	35,760	10,690	20,490
Endogenous sialyl	7,460	14,100	5,530	15,400
Fetuin: galactosyl ‡	17,570	69,000	19,100	42,200
Endogenous galactosyl	40,400	49,200	41,660	31,100
Fetuin: N-acetylglucosaminyl §	9,470	28,170	8,860	24,980
Endogenous N-acetylglucosaminyl	10,320	22,460	13,600	21,890

Enzyme assays were carried out on 0.1% Triton X-100 extracts of the sparse or confluent cells. Details of enzyme assay, preparation of acceptor and complete systems for assay are as given previously^{18,21}. Endogenous activities are without added acceptor in the reaction. Data are means from five experiments.

* Acceptor: Collagen minus glucose¹⁸.

† Acceptor: Fetuin minus N-acetylneuraminic acid¹⁹.

‡ Acceptor: Fetuin minus N-acetylneuraminic acid, galactose²⁰.

§ Acceptor: Fetuin minus N-acetylneuraminic acid, galactose, N-acetylglucosamine²¹.

Roseman¹¹ has postulated that cell surface glycosyl transferases and cell surface acceptors may be responsible for cell to cell adhesion; this postulate has gained some experimental support^{5,12-14}. Cell surface glycosyl ectoenzyme systems were measured in the present cells, and the results are given in Table 5. High levels of activity of surface glycosyl transferase: acceptor reactions were observed in the sparse line 37 cells compared to confluent cultures of both lines and to sparse cells of line 26. Thus the sparse cells of line 37 had much higher levels of surface glycosyl transferase: acceptor activities than line 26 growing either sparsely or at confluency. It should be noted that the high levels of surface enzymes and acceptors in the sparse cells of line 37 may enable them to adhere to surfaces of normal cells, such as platelets^{14,16}, which also have high levels of surface ectoenzymes, or epithelial surfaces containing incomplete glycoproteins, thus contributing to movement of cells during implantation and metastasis. The high levels of surface glycoprotein: glycosyl transferases may contribute to cell

Table 5 Cell Surface Ecto-enzyme Glycosyl-Transferase: Acceptor Reactions

¹⁴ C-labelled precursor	Cell line			
	26	Sparse 37 (c.p.m. per 10 ⁶ cells)	26	Confluent 37
UDP-glucose	497 ± 57	802 ± 235 *	482 ± 61	490 ± 58
UDP-galactose	792 ± 73	2,906 ± 304 *	846 ± 78	929 ± 92
UDP-N-acetylglucosamine	846 ± 88	1,699 ± 108 *	808 ± 42	1,691 ± 104 *
UDP-N-acetylgalactosamine	1,000 ± 218	1,201 ± 192	1,042 ± 181	1,111 ± 162
GDP-fucose	186 ± 27	449 ± 90 *	451 ± 142	488 ± 59
GDP-mannose	802 ± 305	2,015 ± 264 *	912 ± 146	1,040 ± 84
CMP-N-acetylneuraminic acid	953 ± 106	3,423 ± 298 *	948 ± 140	1,410 ± 210

Experiments were performed by collecting cells at sparse state or at confluency by scraping, washing the cells once with 0.1 M Tris (pH 7.6), saline, suspending 0.1 to 0.3 mg as protein of the cells in 0.1 ml Dulbecco's medium without serum, adding 10 µl of 0.1 M MgCl₂, 10 µl of 0.1 M MnCl₂ and 10 µl of a 3.3 µCi ml⁻¹ solution of ¹⁴C-labelled precursor to a final volume of 0.130 ml. The mixtures were incubated for 30 min at 37° C, after which three volumes of 1% phosphotungstic acid in 0.5 N HCl were added and the precipitate was centrifuged out of solution. The precipitate was washed twice with 10% trichloroacetic acid and once with ethanol: diethyl ether (2:1, v/v) and dissolved in 1 N NaOH; radioactivity was determined in a liquid scintillation counter. Data are means ± 1 s.d. from independent observations.

* Significantly different from line 26 ($P < 0.05$).

movement within the circulation by adhering to normal circulating cell surface ectoenzyme systems.

We observed profound changes in the cell surface and in membrane synthetic and degradative enzymes during conditions of sparse growth of a cell line which showed high implantation. When cells were collected at confluency, the high implantation cell line more closely resembled the low implantation line in surface properties; since the cell lines have similar doubling times, cell growth does not seem to be a determinant. It is not known whether these same changes are favoured *in vivo* during periods of sparse growth or whether our findings are applicable to other tumour cell lines. From the data presented here, however, cell surface maturation (or its lack) seems to be a key factor in the cell's ability to implant. Finally, although the extreme differences between the high implantation and low implantation cells seen in the sparse cultures are of interest, the fact that confluent cells of both cell lines are similar has perhaps even greater importance. Even though the genome of line 37 must carry information that makes it have greater potential for implantation and information for extensive cell surface changes, these changes are minimised upon cell contact at confluency and the surface cell properties of cell line 37 become similar to those of cell line 26.

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Inhibition of Carcinogen Formation in Skin irradiated with Ultraviolet Light

THERE is no doubt that sunlight and ultraviolet light cause certain types of skin cancer^{1,2}. Unna first called attention to the high incidence of skin cancer among sailors exposed to sunlight, and his observation on the relationship between the development of skin cancers and exposure to sunlight has been confirmed by many others.

The mechanism of ultraviolet carcinogenesis, however, is not known. We have demonstrated that a mixture of cholesterol-derived photoproducts was present in both human^{3,4} and hairless mouse⁵ skin after exposure to ultraviolet light. Nanogram quantities of cholesterol-derived photoproducts were reported in human skin specimens irradiated with low doses of ultraviolet light. Furthermore, a compound with known carcinogenic properties, cholesterol α -oxide, was identified among those photoproducts. These findings lend support to the hypothesis that photochemical conversion of skin cholesterol to carcinogenic substances may play a role in the induction process of this actinic disease.

Vitamin E, vitamin C and some other biological antioxidants are known to reduce lipid peroxidation damage. Although their relationships are complex, non-biological relationships between antioxidant protective systems and oxidant-labile unsaturated compounds are well established and provide a valuable background for biological study. Here we provide evidence that the formation of cholesterol α -oxide can be inhibited in ultraviolet-irradiated skin by the

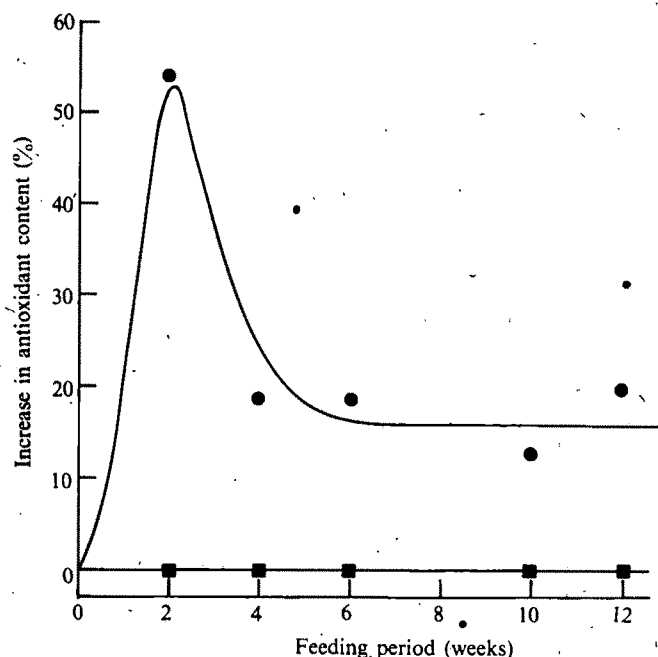


Fig. 1 A comparison of skin antioxidant content between controls and those animals receiving supplemental diets. ■, Controls contained approximately 1.46 μ equivalents antioxidant per g skin and served as baseline levels. ●, % of skin antioxidant levels of animals receiving supplemental diets.

dietary intake of antioxidants and, therefore, suggest a basis for preventive measures against ultraviolet-induced skin cancer.

Female hairless mice (Smith-Meyers strain) were divided into two groups. One group served as controls and received a regular balanced diet. The other group received the regular diet supplemented with the following additives: 1.2% (w/w) ascorbic acid; 0.2% D,L- α -tocopherol powder (250 IU vit E, g⁻¹); 0.1% glutathione (reduced form) and 0.5% butylated hydroxytoluene. Skin was obtained from animals killed at intervals of 2 weeks. The skin specimens were incubated in the presence of 0.3 μ Ci of ³H-(1,2)-cholesterol (specific activity 52.6 Ci mmol⁻¹) suspended in Krebs-Ringer phosphate buffer, pH 7.4, for 18 h at 4° C. The specimens were then rinsed thoroughly to remove exogenous cholesterol and irradiated for 30 min in an environmental chamber maintained at 37° C in an ambient atmosphere. Control skin specimens were treated in an identical manner. Specimens were irradiated through a plane silica lens with a Burdick QA-450N mercury arc lamp (1.43×10^5 erg s⁻¹ cm⁻²).

After irradiation the specimens were homogenised in 10 ml deionised water with a Model 10 Polytron equipped with a saw-toothed generator. The total lipids were extracted with chloroform: methanol (2:1, v/v). Photo-oxidation products in the total lipid extracts were isolated by thin-layer chromatography (TLC). Quantitation of cholesterol α -oxide was accomplished by previously described methods³. Total water-soluble antioxidant content of each skin sample was determined spectrophotometrically by the method of Glavind⁶.

A comparison of skin antioxidant content between controls and those animals receiving supplemental diets for the experimental period can be seen in Fig. 1. Control animals contained an average of 1.46 μ equivalents of antioxidant per g of skin. The maximum increase (54%) in antioxidant content of those animals receiving the supplemental diet occurred in the first 2 weeks of feeding after which the level decreased and was then maintained at approximately 18% above controls.

The antioxidants used in these studies are all known to act

as free radical scavengers and to inhibit lipid peroxidation. The feeding of all four compounds ensured a wide spectrum of antioxidant activity. No gross morphological effects of the skin in those animals receiving the supplemental diet were observed, nor were there noticeable side effects in the animals.

In Fig. 2 it can be seen that the increase in antioxidant content of the skin provided protection against the formation of ultraviolet-induced cholesterol α -oxide. Complete protection against formation of this carcinogen was observed in those animals which had received the supplemental diet for 2 weeks. At this time the maximum increase in skin antioxidant content had occurred. Approximately 50% protection against formation of cholesterol α -oxide was afforded to those animals fed the supplemental diet for 4, 6, and 10 weeks.

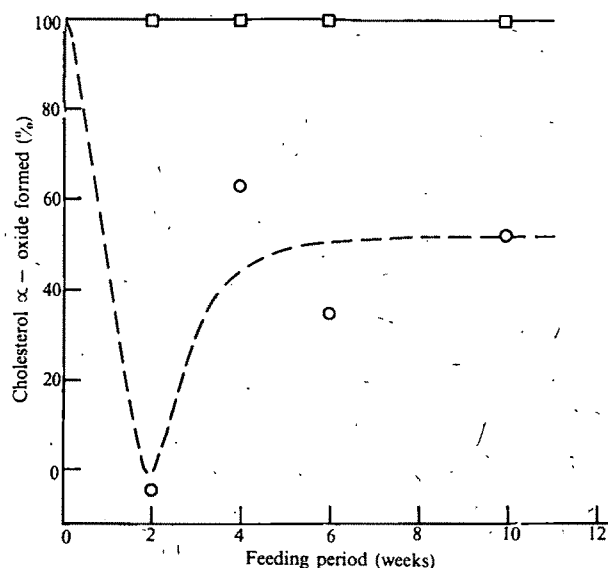


Fig. 2 Inhibition of ultraviolet-induced cholesterol α -oxide in skin. □, Levels of ultraviolet-induced skin cholesterol α -oxide in control specimens after 30 min of irradiation. These levels are represented as 100%. The yield of radiolabelled ultraviolet-induced cholesterol α -oxide after 30 min irradiation is equivalent to approximately 30 ng per g tissue³. ○, % ultraviolet-induced skin cholesterol α -oxide in those animals receiving supplemental diets as compared with controls.

Many protective measures against sunlight and ultraviolet light damage to skin are known. Sun screening agents have been demonstrated to reduce sunburn and skin cancer⁷, but many are far from ideal and there are few that are fully effective⁸⁻¹⁰. In the past numerous compounds have been suggested as possible effective systemic agents against adverse effects of sunlight. Most, however, show toxic effects and their practical systemic use is limited in the prevention of skin cancer. It is obvious that further investigation is needed in order to provide satisfactory protection.

We have now shown that antioxidants, known to impede lipid peroxidation, inhibit the photochemical conversion of skin cholesterol to cholesterol α -oxide. The role of this compound in ultraviolet-induced carcinogenesis is now under investigation¹¹. Moreover, our findings suggest the possible prophylactic effect of systemic antioxidants on the formation of this carcinogen and the subsequent pathological conditions which may result from its formation. Studies related to the prevention of light-induced skin cancer, contingent upon this hypothesis, are presently under way.

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Dietary Enhancement of Intestinal Carcinogenesis by Dimethylhydrazine in Rats

WHILE investigating the effect of marginal lipotrope deficiency in rats on chemical carcinogenesis, we have found an effect in an organ other than liver. We have already reported the enhancement of aflatoxin B₁-induction of hepatocarcinoma by lipotrope deficiency and recently found that N-nitrosodiethylamine and N-nitrosodibutylamine induce hepatocarcinoma earlier and in higher incidence in lipotrope-deficient rats than in normal rats^{1,8}. In the study reported here, induction of tumours of large and small intestine by symmetrical dimethylhydrazine (DMH) was examined in normal or lipotrope-deficient rats and was found to be enhanced in deficient rats.

Male, 4-week-old, Sprague-Dawley rats (Charles River Laboratories) were fed a semisynthetic diet which was either adequate in all known respects for rats (diet 1) or high in fat and marginally deficient in the lipotropes, choline and methionine (diet 2)⁹. After 3 weeks the rats were divided into four groups and given DMH intragastrically: (1) diet 1, DMH 30 mg kg⁻¹ per week for ten doses to twenty-eight rats; (2) diet 2, DMH 30 mg kg⁻¹ per week for ten doses to thirty-one rats; (3) diet 1, DMH 30 mg kg⁻¹ per week for five doses to twenty rats; (4) diet 2, DMH 30 mg kg⁻¹ per week for five doses to

nineteen rats. The five doses were given in 7 weeks and the ten doses in 14 weeks, the weekly dose being omitted in all groups in a week in which weight gain was poor in any one group. After treatment the rats were maintained on their respective diets until they began to bleed heavily from the rectum, developed large tumours of the ear canal, appeared moribund or died. Complete autopsy was performed; tissues were processed for histology by standard methods.

The marginal lipotrope deficiency supports normal or nearly normal weight gain and increases hepatic lipid content only slightly, to $11.3 \pm 1.1\%$ (s.e.) compared with the normal value of $7.5 \pm 0.2\%$. Deficient rats were more sensitive than normal rats to the toxicity of DMH and gained weight more slowly. They therefore received a smaller absolute total dose of the compound. Cumulative probability of death with intestinal tumour, a standardised method of comparing tumour death rates, was calculated from the autopsy data up to 34 weeks after DMH (Fig. 1)⁸. Both diet and dose of DMH influenced the length of time between the first dose of DMH and death with intestinal carcinoma. Deficient rats (diet 2) given the higher dose began to die with tumour 17 weeks after the initiation of treatment, and the curve rose steeply with time. Normal rats (diet 1) given the larger dose began to die with tumour at 21 weeks and also suffered a rapid attrition at an approximately 4-week interval behind the deficient rats. Average life span after the first dose of DMH was 172 ± 6 d (s.e.) for rats fed diet 2 and 195 ± 6 d for rats fed diet 1. The difference is statistically significant, $P < 0.02$. At the smaller dose, deficient rats began to die with tumour at 18 weeks, but the curve rose less steeply than in deficient rats given the higher dose. Normal rats began to die at 23 weeks. Average life span has not been significantly affected by diet in rats given the smaller dose because of the increased incidence of ear duct tumours in rats fed diet 1.

Total mortality up to 40 weeks after the first dose of DMH is given in Table 1. It was the result not only of intestinal tumours but also of ear duct tumours which occurred in greater incidence in the normal rats (Table 1). Of rats fed diet 1 and given the larger dose of DMH, 25% were killed because of signs of intestinal tumours and the remainder because they bore large ear duct tumours. In rats fed diet 2, 66% were killed because of signs of intestinal tumours. At the lower dose of DMH, 45% of rats fed diet 1 and 63% of rats fed diet 2 have been killed because of signs of intestinal tumour. Rats fed lipotrope-deficient diet had twice as many colon tumours per tumour-bearing animal as normal rats at both doses of DMH, but diet did not consistently affect the number of tumours of the small intestine.

Therefore, rats fed the deficient diet were more sensitive to both the toxicity of DMH and its carcinogenicity for the colon as measured by life span between DMH administration and death with intestinal carcinoma, cumulative probability of death with intestinal carcinoma or numbers of colon tumours per tumour-bearing animal. They were significantly less sensitive to DMH carcinogenesis in the ear duct. No significant effect of diet on carcinogenesis in the small intestine was found.

Table 1 Tumour Induction by Dimethylhydrazine in Normal or Lipotrope-deficient Rats

Diet	Total DMH (mg kg ⁻¹)	% Mortality*	% Rats dead with carcinoma of:			No. tumours per tumour-bearing rat in:	
			Colon†	Small intestine†	Ear duct‡	Colon	Small intestine
1	300	100	86	45	75	2.0	1.4
2	300	100	100	55	44	3.7	1.4
1	150	80	56	25	56	1.1	2.0
2	150	68	85	15	15	2.6	1.0

* 40 weeks after initial dose of DMH.

† Adenocarcinoma with varying degrees of differentiation and mucus production.

‡ Squamous carcinoma. Difference between rats fed diet 1 and diet 2 is significant if two doses are combined, $P < 0.05$.

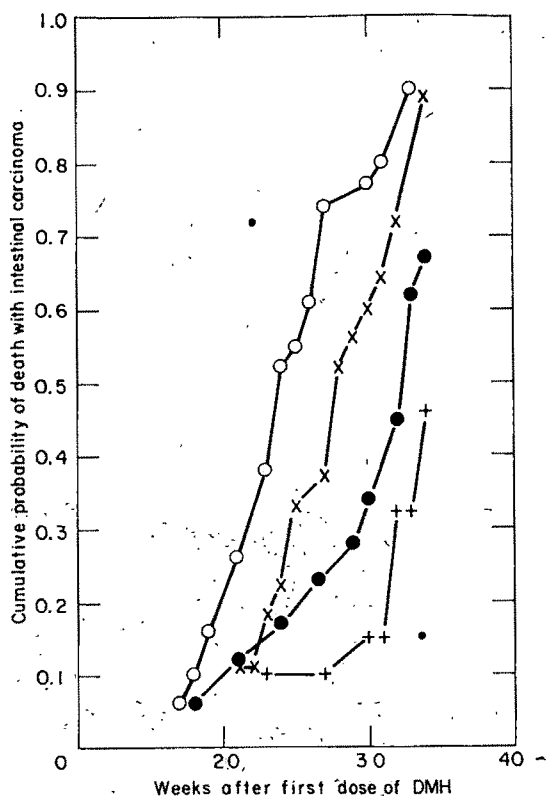


Fig. 1 Cumulative probability of death with intestinal carcinoma in rats fed either adequate diet (diet 1) and given DMH, 30 mg kg⁻¹ for either ten doses (x, twenty-eight rats) or five doses (+, twenty rats) or marginally lipotrope-deficient diet (diet 2) and given DMH, 30 mg kg⁻¹ for either ten doses (o, thirty-one rats) or five doses (●, nineteen rats).

This suggests that the dietary effect is exerted in the colon itself, either directly on the mucosa or indirectly by altering bacterial flora and its metabolism of the carcinogen.

Diet has been postulated to be responsible for the marked geographic variations in human colon carcinoma. Both dietary fat and carbohydrate have been incriminated^{4,5}. In experimental studies we have found that vitamin A deficiency enhances induction of colon carcinoma by aflatoxin B₁ but not by DMH^{6,7}. The study reported here has demonstrated enhancement of DMH induction of intestinal carcinoma by lipotrope deficiency. Whether the effect is due to the deficiency *per se* or to the high fat content of the diet used to induce it must be answered by further studies.

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"Asian Cigarette" is an Adverse Prognostic Factor in Peripheral Arterial Disease

In parts of South East Asia physicians believe that the strong, inexpensive locally made cigarettes are a risk factor in the development of peripheral arterial disease. Thus, in Ceylon the young men who smoke Beedi cigarettes are said to be particularly prone to occlusive diseases of the small arteries¹. A study of the Buerger syndrome in Korea revealed that the patients smoked a coarse form of locally grown tobacco². In other parts of Asia where the Buerger syndrome has been described the disease predominates in the lowest socio-economic groups (N. K. Yong, personal communication, and refs 3 and 4). Presumably, these poor people smoke the locally grown and locally manufactured cigarettes most often since they are the cheapest available.

In a recent epidemiological study of a large number of patients with the Buerger syndrome in Indonesia the patients were found to smoke cigarettes of three basic types³. The commonest was 'Kawung', the tobacco of which is grown, air cured and prepared at home by the patients or their neighbours. It is a coarse form of tobacco rolled in a tissue made from the leaves of the sugar palm and is the cheapest type of cigarette available in Indonesia. 'Kretek' cigarettes are made from a better quality, commercially available tobacco mixed with cloves and spices and wrapped in a normal tissue as used in Western cigarettes. 'Western'-type cigarettes were also smoked by these poor patients as were also conglomerates of tobacco removed from discarded cigarette butts and remanufactured by some enterprising merchant.

Because there was no information available about the smoking habits of the controls at a time comparable to the onset of the disease in the patients they were matched with, we are not able to comment on the Kawung cigarette as a risk factor.

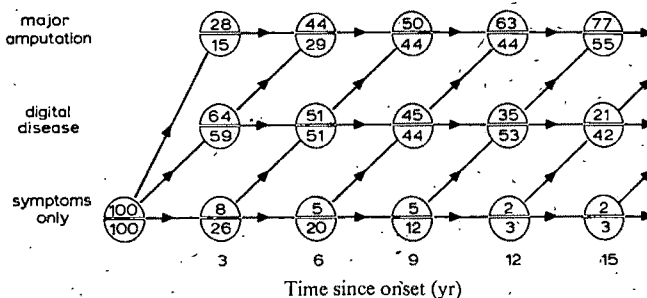


Fig. 1 State flow chart showing the expected clinical course of Buerger's disease in 100 patients who smoked Kawung cigarettes (upper half circles) compared with the expected clinical course in 100 patients who did not smoke Kawung cigarettes (lower half circles).

In Fig. 1, however, a state flow chart describes the expected clinical course for 100 Indonesian patients with Buerger's disease who smoked Kawung cigarettes, and compares it with the expected clinical course for 100 patients who smoked Kretek cigarettes, Western cigarettes or a combination of these two. At each time interval, during the course of the disease for the group of patients, Kawung cigarettes are associated with a worse prognosis. The state flow chart is derived from a mathematical model of Buerger's disease and the theoretical aspects are detailed elsewhere^{6,7}.

Although we found that Kawung smoking was associated with a low socio-economic status, which in itself was found to be an adverse prognostic factor, it was also found that Kawung smokers of higher socio-economic status had just as poor a prognosis as Kawung smokers of low socio-economic status.

Furthermore Kawung smokers were not found to be heavier smokers than the other patients⁷.

These findings are in accord with the opinion of Indonesian physicians who feel that the cheap Kawung cigarette is both an important risk factor and an important prognostic factor for Buerger's disease. Our findings also lend weight to the clinical impression of doctors throughout South East Asia that local cheap home-made cigarettes are often associated with the development of peripheral vascular disease and also with a worse prognosis than Western-type cigarettes.

We suggest that it may be of some value to examine more closely the Asian cigarette and especially the Indonesian Kawung cigarette which has been shown to be directly associated with a worse prognosis in at least one type of peripheral vascular disease. More epidemiological and clinical data are needed as well as direct information about the cigarettes themselves. As far as we are aware the nicotine content of the Kawung cigarette is unknown and carboxyhaemoglobin levels in Kawung smokers have not been studied.

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Antibodies to α -Foetoprotein cause Foetal Mortality in Rabbits

α -FOETOPROTEINS (AFP) have been observed in the serum of all mammalian species so far studied^{1,2}. In the rabbit AFP constitutes about 33% of the total serum protein on day 20 of gestation and reaches a peak concentration around days 24 to 26 (ref. 3). This ontogenic pattern is similar to that of the rat where maximum concentration is also reached late in gestation, but differs from the human where a steady decline occurs after the first trimester^{4,5}. Although considerable interest has attached to the reappearance of AFP in the serum of adult animals and human patients with hepatocellular cancer⁶⁻⁹, little attention has been given to the possible role of this protein in normal development. The preliminary experiments reported here were designed to investigate this aspect by selectively neutralising AFP *in vivo* with specific antibodies.

Dutch rabbits in their first pregnancy were injected intravenously on the twenty-first day of gestation with 2 ml per kg body weight of high titre sheep anti-AFP¹⁰; control animals received similar doses of normal sheep serum. The animals were killed 24 h later and the condition of the foetuses was examined. The results are summarised in Table 1.

There was a very high incidence of foetal mortality in animals injected with anti-AFP. The extraembryonic fluids of the dead foetuses were invariably contaminated with blood, and the yolk sac was fragile and translucent showing no vitelline circulation. Most of the foetuses that were

Table 1 Foetal Mortality

Rabbit	No. of foetuses		Left		No. dead	%
	Left	Right	Left	Right		
1	4	4	4	4		100
2	8	3	5	2		63.5
3	2	7	0	2		22
4	2	4	2	4		100
5	1	4	1	1		40
C ¹	4	3	0	0		0
C ²	2	2	0	0		0

C¹ and C² were controls.

alive looked healthy although one or two showed signs of superficial haemorrhage. Analysis of the uterine fluid revealed the presence of sheep antibodies. These were also present in the exocoelomic fluid of both live and dead foetuses, appreciably more being present in the latter. The amniotic and allantoic fluids and the foetal serum were consistently negative for sheep antibodies in both live and dead foetuses.

Previous studies have shown the importance of the yolk sac as a primary site of AFP synthesis in the rabbit^{10,11} and in the rat¹² and human¹³. It is also well established that the yolk sac plays an important role in the transmission of maternal antibodies to the foetus in rabbit and rodents¹⁴, as well as subserving other important functions during development¹⁵. In view of the fact that sheep antibodies are poorly transmitted to the rabbit foetus¹⁴ and that no evidence could be found for their presence in the foetal serum here, it seems unlikely that the anti-AFP was exerting its effect on the embryo directly, although this possibility cannot be entirely discounted. It seems more probable that the site of action was the yolk sac, but whether foetal death resulted from a specific deficiency of AFP or a more general impairment of yolk sac function cannot as yet be concluded. The fact that some foetuses survived apparently unharmed presumably reflects either a differential exposure to the antibody or variation in susceptibility to its action. Studies are currently in progress to try to resolve these problems.

Antibodies directed towards the yolk sac are known to produce congenital malformations and foetal mortality in pregnant rats¹⁶, and *in vitro* studies have demonstrated that the primary action is on the visceral yolk sac rather than on the embryo directly and is independent of any immunological reaction of the mother¹⁷. A similar explanation would seem appropriate for the results presented here; indeed, it is not improbable that at least one of the active components in yolk sac antiserum is directed towards AFP.

Antibodies to AFP clearly have disastrous effects on the foetus and it is relevant to speculate whether some congenital malformations and abortions may be due to maternal isoimmunisation.

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Serum Progestins and Luteinising Hormone Levels in Non-suckled Primiparous Heifers

PRIMIPAROUS heifers normally have a longer interval from parturition to oestrus, ovulation and subsequent conception than do mature cows. Lactation also extends this interval. We have therefore measured simultaneously luteinising hormone (LH) and individual progestins within the same serum sample throughout the postpartum interval in the bovine species in order to elucidate the endocrine events that occur before the first oestrus.

In Fig. 1, the horizontal scale from -24 reveals a similar ovarian and endocrine pattern preceding oestrus for the three non-suckled primiparous heifers. The interval from parturition to first oestrus for heifers 1, 2 and 3 (Fig. 1) was 22.75, 27.75 and 35.75 d, respectively.

Cyclic follicular activity was recorded throughout the postpartum interval for each heifer and follicular growth was intensified for several days preceding oestrus. Ovulation with subsequent corpus luteum formation occurred on the left, right and right ovaries, respectively, for heifers 1, 2 and 3.

Increased levels of LH were observed for the length of approximately one cycle (day -17 to day -20) before oestrus; thereafter, LH remained at low levels until oestrus. A typical LH peak coincided with oestrus for all three heifers, reaching 13.3, 11.0 and 65.0 ng ml⁻¹, respectively. The LH peak observed at oestrus agrees with other reports (ref. 6 and personal communication from J. N. Wiltbank).

Sustained 4-pregnene-3,20-dione (P) and 20 β -hydroxy-4-pregnene-3-one (20 β -OHP) release from undetectable levels occurred several days before oestrus for all three heifers. The increased levels of P and 20 β -OHP preceding oestrus differed among the three heifers as to duration of release and levels.

Auxiliary peaks of 17-hydroxy-4-pregnene-3,20-dione (17-OHP) were observed before the major P and 20 β -OHP release for heifers 1 and 3. In all three heifers, increased levels of 17-OHP occurred during the time of increased serum P and 20 β -OHP release. A significant 17-OHP peak occurred at or near oestrus for all three heifers. Not until both P and 20 β -OHP had reached a very low serum level before oestrus did the 17-OHP and LH peak occur. It is interesting that a second 17-OHP peak occurred after oestrus, near ovulation, for heifer 3. This 17-OHP peak near ovulation has also been observed for the heifer exhibiting a normal oestrus cycle (unpublished results of R. L. T., D. T. Atkins and J. L. F.).

Plasma progestin levels of approximately 1 ng ml⁻¹ have been reported in the postpartum cow, with a level of slightly over 2 ng ml⁻¹ 7 d before first oestrus (ref. 6 and personal communication from J. N. Wiltbank). Some workers have reported increased elevation of P levels 3 to 5 d before the first postpartum oestrus, whereas others found postpartum plasma P levels to be present in a cyclic pattern within 20 d postpartum, similar to that observed for non-pregnant mature cows⁸. In two cows in which the P analysis was

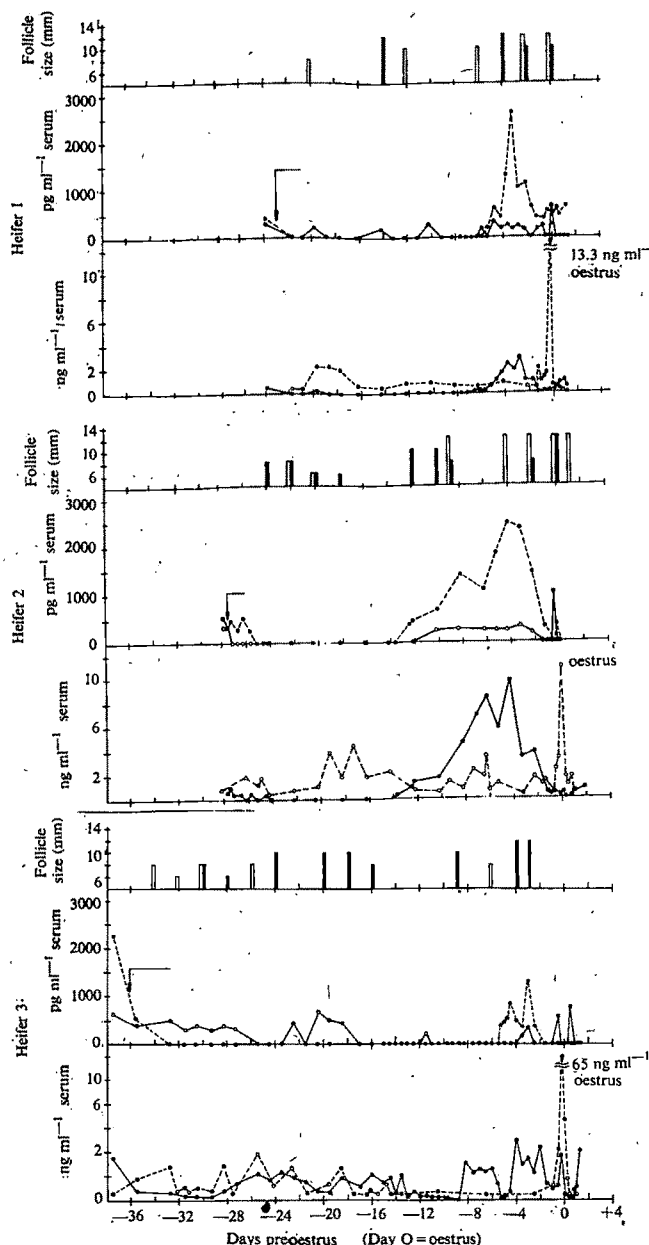


Fig. 1 Results obtained from three non-suckled Hereford heifers (1, 2 and 3) from parturition to first oestrus postpartum. Indwelling jugular cannulas were inserted into these heifers approximately 2 weeks before calving to expedite procuring multiple blood samples. Samples of 20 ml of blood were collected at intervals of 6 h through parturition to the first postpartum oestrus. At each of these blood collections, oestrus was detected with the aid of a penicillated bull. The blood was allowed to clot at room temperature and the serum was frozen. Blood cellular components were monitored periodically to determine the health of the animal. Calves were removed from these heifers immediately after birth. All heifers were palpated every second day to determine ovarian activity and gross uterine involution rate. Undetectable levels of the hormones are plotted on the base line. Note that both 20 β -hydroxy-4-pregnene-3-one (20 β -OHP) and 17-hydroxy-4-pregnene-3,20-dione (17-OHP) are in units of ng ml⁻¹, whereas LH and 4-pregnene-3,20-dione (P) are in units of pg ml⁻¹. LH was radioimmunoassayed by the double-antibody technique⁴ using bovine LH (NIH-LH-B8) as the standard. Both P and 17-OHP were measured by radioimmunoassay using an antibody directed against 11-deoxycortisol^{2,3}. Serum (1 ml) was extracted with ether and P, 20 β -OHP and 17-OHP were separated on a micro-Celite column⁴. The 20 β -OHP was quantitated as P after enzymatic oxidation⁵ and resubmission to the 'Celite' column. Black columns, right ovary; white columns, left ovary. For each heifer the upper graphs represent: ●---●, 20 β -OHP; ○---○, 17-OHP; and the lower graphs represent: ●---●, P; ○---○, LH (NIH-LH-B8). The arrows indicate parturition.

carried to the first postpartum oestrus, an increase in P from approximately 0.20 ng ml^{-1} to a peak of approximately 1 ng ml^{-1} preceded oestrus by a few days⁸. Echternkamp⁹ found in lactating Holstein cows that plasma P values remained at low basal levels (0.0 to 0.3 ng ml^{-1}) until the first oestrus postpartum. Robertson¹⁰ reported that auxiliary plasma P peaks occurred before the first postpartum mucous discharge in cows and was uncertain whether these P peaks were preceded by ovulation or whether they were derived from luteinised follicles.

The "two cell theory", described in the bovine species^{11,12}, postulates that the theca interna has the enzymes to convert P to oestrogen which is representative of follicular activity, with no apparent 20β -hydroxysteroid dehydrogenase (20β -HSD), whereas other workers¹³ have found that 20β -HSD activity resides in both the granulosa and theca cell layers. The luteinised granulosa cell which is representative of luteal activity lacks the 17 -hydroxylating enzyme, but has 20β -HSD¹¹⁻¹³. Other researchers have confirmed the findings observed for the "two cell theory", isolating P and 17 -OHP in follicular fluid¹⁴, whereas only P and 20β -OHP were found in luteal tissue¹⁵ with very little, if any, ability to aromatise C-19 steroid precursors into oestrogens¹⁶.

In our study, increased LH levels were observed before the onset of P release and the P levels and time duration data follow a pattern similar to the mature cow. The facts that neither oestrus, ovulation nor corpus luteum formation was observed before P release, and that 20β -OHP was present, suggest that a follicle was luteinised. Others^{18,17} found with the bovine species that luteinisation of both theca and granulosa cells of preovulatory follicles began before ovulation. LH can cause pseudoluteinisation of non-ovulatory follicles and (or) cause ovulation of mature follicles in humans¹⁹. The granulosa cell layer of luteinised follicles from rabbits synthesises as much P as do the corpora lutea of pseudopregnant rabbits²⁰. The oocyte itself and (or) high levels of LH induce luteinisation, which determines the specific steroid hormones produced in the rat²¹.

We believe that this is the first report of monitoring of bovine blood levels of 17 -OHP. High levels have been found in follicular fluid, but not in the corpus luteum or ovarian stroma¹⁴. The presence of the peak 17 -OHP observed before ovulation for the three heifers suggests that 17 -OHP serves a role similar to that observed in women, where ovarian venous²² and peripheral plasma levels^{23,24} of 17 -OHP begin to increase 3 d before ovulation and peak coincident with the mid-cycle LH peak. The 17 -OHP level has been shown to be the highest in the human ovary bearing the mature follicle²². It has been postulated that both oestradiol- 17β and 17 -OHP have to be present in order to achieve the mid-cycle surge of gonadotrophins in women necessary for ovulation²⁵. Likewise, an increase in 17 -OHP and oestradiol- 17β has been reported in equine follicular fluid just before ovulation²⁶. A pharmacological dose (20 mg per cow) of 17 -OHP injected into ovariectomised dairy heifers, however, had no detectable effect on LH levels²⁷.

Low levels of P seem to be necessary for LH synthesis and (or) release in the bovine female²⁸. Investigators have postulated that in the human female, constant, slowly changing, or high levels of P inhibit both tonic and surge LH, while low, rapidly increasing levels have a net stimulatory effect^{18,29}.

Our preliminary findings on the endocrine events preceding the re-establishment of normal cyclic activity in three non-suckled postpartum heifers demonstrate increased LH levels 17 to 20 d before oestrus, which is succeeded by a dramatic synthesis and (or) release of P and 20β -OHP for several days preceding the LH peak at the time of oestrus. At present, no specific role of 20β -OHP has been identified for the bovine female. There is strong evidence that its α -epimer, 20α -hydroxy-4-pregnen-3-one, acts as a positive feedback mechanism for LH discharge in the rat³⁰ and rabbit³¹.

Perhaps 20β -OHP is required to return the biological system to its normal cyclic pattern.

An improved understanding of the endocrinological changes associated with the postpartum interval should be beneficial in formulating means of decreasing this interval, thereby allowing an increase in the life-time production of the cow. Although our data in this communication are derived from three heifers, we are confident that the result is a common phenomenon.

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Is Cortisol Responsible for Inhibition of MLC Reactions by Pregnancy Plasma?

THE foetus inherits histocompatibility antigens from the father and becomes an allograft to the mother, but is not rejected. Possible reasons for this have been discussed by Billingham¹. Various hypotheses, including a physiological barrier between the mother and the foetus and a reduction of the immunological reactivity of the mother during pregnancy, have been suggested. I recently reported the inhibitory effect of pregnancy plasma on the mixed leukocyte culture (MLC), which I believe not to be mediated by an antibody but possibly by the particular hormonal situation of pregnancy². Here I report experiments to study whether 17-hydroxycorticosteroids are inhibitory factors in pregnancy plasma. I studied the inhibitory activity on the MLC reactivity of plasma taken at various intervals during pregnancy and measured the plasma cortisol level of each specimen.

Blood samples were obtained from fifteen primiparous mothers immediately after delivery and from fifty-five primigravidas at the tenth and thirty-ninth weeks of gestation. Control plasmas were obtained from healthy adult females who had no history of pregnancy or blood transfusion. Cell-free plasmas were prepared from these heparinised blood samples (preservative-free heparin, 200 units per 10 ml blood) and frozen at -20°C until tested.

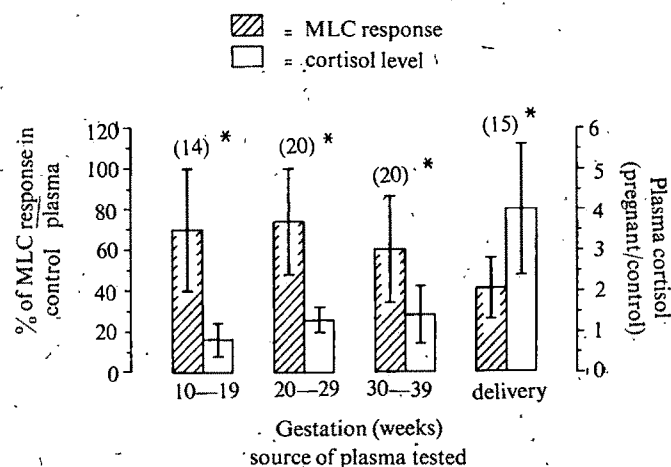


Fig. 1 Inhibitory activity of plasmas from primigravidas at various weeks of gestation and level of cortisol in these plasmas. In each experiment, five aliquots of MLC were prepared from a given pair. Each aliquot was suspended separately in test plasma of each group and in control plasma. Reactivity (c.p.m.) of MLC suspended in each test plasma is expressed as percentage of MLC reactivity in control plasma. The level of cortisol is expressed as the ratio of cortisol concentration of test plasma to that of control plasma. Mean values and s.d. are depicted. * = Number of experiments in each group.

Leukocyte suspensions were prepared from normal volunteers, unrelated to one another. Preparation of leukocyte cultures and measurement of the incorporation of ^3H -thymidine into DNA have been described before². Donor leukocytes were resuspended in frozen stored pregnancy and control plasmas. The plasma containing the leukocytes was diluted with medium 199 so that the final plasma concentration was 20%. The cell suspensions were incubated in 17×100 mm disposable plastic tubes. The mixed cultures contained a 1:1 mixture of cells from two subjects in test pregnancy and control plasmas. The cultures were incubated at 37°C for 7 d. At the end of the incubation period, ^3H -thymidine (specific activity 5.0 Ci mmol^{-1}) was added to each tube to give a concentration of $1.0 \mu\text{Ci ml}^{-1}$. The

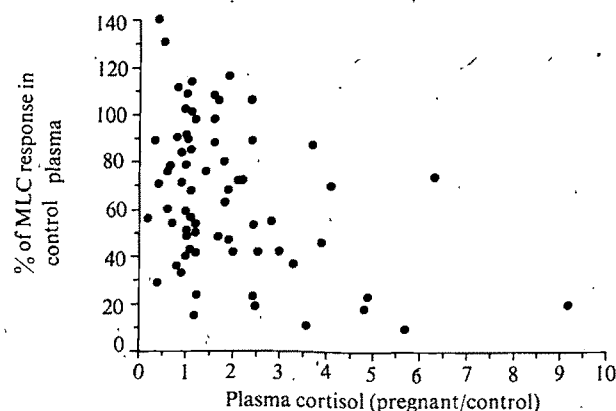


Fig. 2 Relationship of the inhibitory activity to the level of cortisol in the plasma of primigravidas, expressed as in Fig. 1. Dots represent the individual samples.

amount of ^3H -thymidine taken up was measured after incubation for 4 h.

The plasma cortisol level was determined by using the steroid-binding properties of cortisol-binding globulins³. In this study the range of cortisol levels in control plasma was $5-29 \mu\text{g}$ per 100 ml plasma.

Figures 1 and 2, and Table 1, show the relationship of inhibitory activity of pregnancy plasmas on the MLC reactivity to concentration of cortisol in these plasmas. Table 1 shows the results from five experiments, typical of the fourteen experiments performed. In each experiment, six aliquots of MLC were prepared from a given pair. Each aliquot was suspended separately in plasmas from six females, five of whom were pregnant. This experiment was repeated a total of fourteen times, always with different leukocytes and plasmas. As shown previously², most pregnancy plasmas were inhibitory to the reactivity of MLC. Their inhibitory activity was maximal at the time of delivery. The level of cortisol in pregnancy plasma rose during pregnancy and reached a maximum at the time of delivery.

Table 1 Effect of Pregnancy Plasma on Mixed Leukocyte Reaction

Experiment No.	^3H -thymidine uptake in cultures of mixed leukocytes from unrelated donors					
	Control plasma*	Pregnancy plasma† (gestation in weeks)				
		10-19	20-29	30-34	35-39	Delivery
1	27,388† (22.0)§	15,660 (13.9)	12,579 (21.6)	12,806 (28.8)	9,051 (35.2)	3,492 (65.3)
2	23,529 (17.0)	24,821 (9.0)	18,949 (33.1)	16,334 (40.9)	19,443 (36.5)	14,389 (69.3)
3	46,220 (17.4)	30,808 (21.3)	21,801 (33.5)	19,315 (31.8)	16,845 (30.8)	15,632 (50.8)
4	20,181 (22.5)	15,503 (18.4)	9,213 (25.0)	10,659 (22.9)	12,079 (57.0)	3,736 (81.3)
5	27,667 (12.0)	25,396 (20.4)	18,969 (25.4)	19,642 (26.3)	8,736 (52.5)	11,642 (75.0)

* Control plasmas were obtained from healthy adult females who had no previous history of pregnancy or blood transfusion.

† Pregnancy plasmas were obtained from primigravidas at various weeks of gestation and after delivery. Different plasmas were tested in different experiments.

‡ C.p.m. per culture; mean from triplicate cultures.

§ Plasma cortisol level (μg per 100 ml plasma).

The mean values of inhibitory activity and cortisol level shown in Fig. 1 for each period of pregnancy suggested a correlation between inhibitory activity of pregnancy plasmas and the concentration of cortisol in these plasmas. Plotted as individual points (Fig. 2), there was no exact correlation between the inhibitory activity and cortisol content of each

pregnancy plasma. Within each experiment the pregnancy plasmas which contained the highest levels of cortisol were not necessarily the most inhibitory to the MLC reactivity. A correlation analysis was done for the data to examine the crude and partial correlations between MLC reactivity (c.p.m.), period of gestation (in weeks: non-pregnant control at zero time), and cortisol concentration (μg per 100 ml plasma). The data from each experiment were treated separately. The correlation coefficient for MLC inhibition and period of gestation was highly significant ($r = -0.63$; $P < 0.001$). The correlation coefficient for MLC inhibition and cortisol concentration was also highly significant ($r = -0.49$; $P < 0.001$). Since cortisol concentration was closely correlated with gestation time ($r = -0.61$; $P < 0.001$), a partial correlation analysis was, however, done to eliminate the effect of gestation time. When this was done, the individual partial correlations of MLC inhibition with cortisol concentration were inconsistent (ten negative; four positive), and the pooled coefficient was not significantly different from zero ($r = -0.18$; $P > 0.1$). Thus it seems that although the period of gestation is correlated with the degree of MLC inhibition, there is no close correlation between cortisol concentration and MLC inhibition.

Table 2 Effect of Temperature (60°C) on Inhibitory Activity of Pregnancy Plasma

Experiment No.	^3H -thymidine uptake ($\times 10^{-3}$) in mixed leukocyte cultures* containing			
	Untreated Control plasma	Pregnancy plasma	Incubated at 60°C for 1 h Control plasma	Pregnancy plasma
1	$34.3 \pm 4.9 \dagger$	21.0 ± 5.6 (61%)§	17.0 ± 4.8	8.4 ± 1.8 (49%)
2	21.5 ± 1.6	8.4 ± 1.5 (39%)	23.5 ± 1.7	9.4 ± 1.6 (40%)
3	27.9 ± 2.2	6.9 ± 1.4 (25%)	23.1 ± 6.5	6.6 ± 0.6 (28%)
4	27.7 ± 1.7	11.6 ± 3.4 (42%)	20.6 ± 2.4	8.2 ± 1.2 (40%)
5	18.6 ± 2.2	8.4 ± 2.7 (46%)	16.4 ± 1.0	6.9 ± 1.7 (42%)

* In different experiments, mixed leukocyte cultures were prepared using different pairs of unrelated donors.

† Plasmas from primiparas immediately after delivery. Different plasmas were tested in different experiments.

‡ C.p.m. per culture; mean from triplicate cultures $\pm$ s.d.

§ Figures in parentheses indicate a percentage of the reactivity of MLC in control plasma.

Table 2 shows the effect of temperature (60°C) on the inhibitory activity of pregnancy plasma on the reactivity of MLC. Incubating pregnancy plasma at 60°C for 1 h had no effect on its inhibitory activity.

I have thus shown that cortisol is not a major inhibitory factor in pregnancy plasma. Unbound cortisol is considered to be the biologically active portion of the total plasma cortisol⁴, but reliable techniques are not readily available for measuring unbound cortisol. Therefore, I measured the total plasma cortisol. A parallel increase in the concentration of total plasma cortisol and its unbound fraction during pregnancy has been shown⁴.

At present, the nature of this inhibitory factor in pregnancy plasma is unknown. Ceppellini⁵ and Leventhal *et al.*⁶ have shown that an antibody is present in multigravida female plasma that is directed against HL-A specificities of stimulating cells and decreases their capacity to stimulate in MLC. Our inhibitory factor is unlikely to be an antibody against HL-A specificities for the following reasons: first, in this study, none of the test pregnancy plasmas were cytotoxic toward donor lymphocytes used in MLC by conventional assay techniques using rabbit serum as a source of complement⁷. Second, most pregnancy plasmas tested

inhibited the reactivity of MLC from unrelated pairs that were selected at random in each experiment.

Gatti *et al.*⁸ have found an inhibitory factor of MLC reactions in serum from a healthy multigravida female. Their factor contains the 7S IgG fraction and has the broad specificities, but it is not lymphocytotoxic or directed against HL-A specificities. While our inhibitory factor disappears shortly after termination of pregnancy², in their study inhibitory activity persists in the donor's serum 16 months after delivery of her last child⁸.

Stimson⁹ has suggested that a serum macroglobulin present in pregnancy sera (pregnancy-associated globulin) may be an immunosuppressive globulin. Horne *et al.*¹⁰ have, however, been unable to demonstrate that sera containing measurable quantities of this globulin have a depressive effect on the mitogenic response following phytohaemagglutinin (PHA) or tuberculin purified protein derivative (PPD) stimulation of lymphocytes. My inhibitory factor differs from this globulin. While this globulin is completely inactivated by heating the positive serum at 60°C for 10 min¹¹, my inhibitory factor is resistant to incubation at 60°C for 1 h (Table 2). I think that, rather than an antibody, progesterone, oestrogen and/or human chorionic somatomammotrophin (HCS) may be responsible for inhibitory activity. Progesterone and oestrogens show immunosuppressive properties as measured by prolonged allograft survival^{12,13}. It has also been shown that HCS suppresses PHA-induced lymphocyte transformation¹⁴.

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Animal Model to Study the Relationship between Immunoreactive Gastrin and Inflammatory Arthritis

THE observation of raised concentrations of radioimmuno-reactive gastrin in the plasma of patients with rheumatoid arthritis¹ has directed attention to the role of this foregut hormone in the inflammatory response. Evaluation

of the significance of this relationship would be simplified if a suitable animal model were available. We have studied immunoreactive gastrin in rats following the induction of adjuvant arthritis in an attempt to establish such a model.

A series of twenty-two adult male Sprague-Dawley rats was studied. Adjuvant arthritis was induced by subplantar injection of 0.5 mg killed *Mycobacterium butyricum* in 0.1 ml heavy mineral oil (adjuvant) into the left hind paw. The progress and severity of the arthritis were monitored by paw scores and by weight reduction in the affected animals. These assessments were carried out immediately before letting blood for gastrin assay on the day before injection of adjuvant and on the fourteenth day following injection.

Plasma gastrin was measured in venous blood samples, using a sensitive and specific radioimmunoassay following a 15 h overnight fast. This assay is based on antibody raised in rabbits to synthetic human gastrin. Labelled hormone is prepared using a modification of the chloramine-T method of Hunter and Greenwood² and separation of the free hormone from that bound to antibody is achieved with dextran-coated charcoal³. Precision of this assay is greatest below 600 pg ml⁻¹ and the lowest concentration of gastrin which can be detected is of the order of 10 pg ml⁻¹. Cross-reaction with cholecystokinin and pancreozymin is minimal and preliminary studies indicate that the antibody recognises not only the heptadecapeptide hormone but also the 'big' gastrin described by Yalow and Berson⁴.

The mean weight of the seventeen normal rats was 306.6 ± 5.1 g (s.e.m.) and of the thirteen injected rats was 293.8 ± 7.2 g (s.e.m.).

The mean radioimmunoreactive gastrin level in the untreated group was 234.6 ± 35.9 pg ml⁻¹ (s.e.m.) and that of the adjuvant group was 401.4 ± 41.7 pg ml⁻¹ (s.e.m.). The difference between the two groups is statistically significant ($t=2.91$; $0.01 > P > 0.001$).

Table 1 Weight, Paw Scores and Gastrin Concentrations in Rats Before and After Injections of Adjuvant

Rat	Pre-adjuvant			Post-adjuvant		
	Weight (g)	Paw score (0-5)	Gastrin (pg ml ⁻¹)	Weight (g)	Paw score (0-5)	Gastrin (pg ml ⁻¹)
6	300	0	120	275	3	505
8	300	0	405	250	2	455
10	355	0	130	325	3	790
13	325	0	355	300	5	470
16	295	0	245	250	2	610
17	310	0	135	275	1	610
19	310	0	215	270	2	230
20	300	0	90	325	1	160
Mean	311.8		211.8	283.7		478.7
± s.e.m.	± 7.0		± 41.1	± 10.5		± 72.7

In eight rats it was possible to measure immunoreactive gastrin both before and after the successful induction of adjuvant arthritis (Table 1). The initial mean weight of this group of rats was 311.8 ± 7.09 (s.e.m.) and the weight of all but one of these animals dropped after adjuvant administration to a mean of 283 ± 10.5 g (s.e.m.). This drop is statistically significant ($t=3.415$; $0.02 > P > 0.01$). The initial mean gastrin concentration of this group was 211.8 ± 41.1 pg ml⁻¹ (s.e.m.). Fasting gastrin rose in all animals following adjuvant, to a mean value of 478.7 ± 27 pg ml⁻¹ (s.e.m.). This rise is also statistically significant ($t=3.182$; $0.05 > P > 0.02$). It seems clear that adjuvant arthritis in rats is associated with an elevation of fasting plasma immunoreactive gastrin, providing a suitable model for further work on the significance of this hormone in the inflammatory process.

One criticism of the observation of raised serum immunoreactive gastrin in patients with rheumatoid arthritis¹ arose from the very real possibility that the phenomenon was produced by the drugs which the patients were receiving. In the light of our present results from untreated adjuvant rats it now seems unlikely that high gastrin levels are a consequence of drug therapy.

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IQ and ABO Blood Groups

THREE methods are available for the genetic analysis of continuous variables in human populations. One is the biometrical approach¹ which, in addition to partitioning the phenotypic variance into genetic and environmental components, has been used to reveal sex linkage² and provide estimates of the number of effective factors³. Second, genetic markers can be studied for evidence of pleiotropic effects⁴, and third, linkages between polygenic factors and segregating genetic markers can be sought^{5,6}. It is not always possible to distinguish between linkage and pleiotropy, so the second and third methods need similar data and thus go together.

In spite of the availability of segregating genetic markers, techniques for the location of polygenes⁷, developed in *Drosophila*⁸ but also very successful in mice⁹ and wheat¹⁰, have not been applied to human material. We are attempting to do so, and as a result have found an association between IQ and ABO blood group phenotypes. We have data for more continuous variables and more marker genes but the association reported here comes from the first system we have analysed.

The sample population comprised males and females between the ages of 18 and 70 living in six ecclesiastical parishes in Otmoor, a region some 5 to 10 miles north-east of Oxford¹¹. Age corrected IQs, measured on the Wechsler Adult Intelligence Scale¹², and ABO blood group phenotypes are available for 534 individuals. The sample was collected in seven villages on a house-to-house basis and contains some individuals known to be related to one another.

The data (Table 1) show significant differences in mean IQ between some of the ABO phenotypes. In particular the A₂ group has the highest mean IQ and the A₂ and the O phenotypes each have significantly higher mean IQs than the A₁ phenotype.

Table 1 Mean IQs of the ABO Phenotypes

	A ₁	A ₂	B	O	A ₁ B	A ₂ B
n	263	25	43	271	12	6
mean IQ	106.95	111.16	107.25	109.75	107.58	111.16
s.e.m.	0.72	2.01	1.86	0.67	2.21	5.2

The difference in mean IQ between the O and A₁ phenotypes observed overall is significant in the data from four of the seven villages (Table 2). Of the other three there is no difference in Beckley, but Horton, which is characterised by the highest mean IQ, seems to stand out because the direction of the difference is the other way round. This is not, however, significant. Further, the data for the seven villages provided no statistical evidence for heterogeneity in the differences in mean IQ between the O and A₁ phenotypes ($\chi^2_6=11.3$, $P>0.05$). Unfortunately the number of A₂ phenotypes in the sample is too small to allow comparisons to be made between the villages.

Table 2 Mean IQs of the A₁ and O Phenotypes in the Seven Villages

	A ₁	O	Difference in mean IQ between A ₁ and O		Probability
Horton	115.89 (46)*	111.51 (47)	-4.38	$t_{91}=1.6$	NS
Merton	107.71 (28)	112.57 (37)	+4.86	$t_{63}=2.1$	0.05
Beckley	109.68 (38)	109.60 (42)	-0.08	$t_{78}=0.04$	NS
Wendlebury	105.41 (49)	111.64 (50)	+6.23	$t_{97}=2.4$	0.05 > $P>0.01$
Weston	104.09 (32)	108.28 (29)	+4.19	$t_{59}=1.98$	0.05
Charlton	101.16 (57)	106.00 (55)	+4.84	$t_{110}=2.4$	0.05 > $P>0.01$
Boarstall	103.92 (13)	107.82 (11)	+3.90	$t_{22}=0.81$	NS

* Sample sizes given in parentheses.
NS=not significant.

Charlton was the first village for which complete data were available and analysed and they showed a significant difference in mean IQ between the O and A₁ phenotypes. As associations of this kind are notoriously suspect as statistical artefacts it was prudent to use the Charlton data to provide a hypothesis which could be tested by the data obtained from the six other villages, which were collected and analysed later. If the Charlton data are excluded from the analysis the remainder still show a significant difference in mean IQ between the O and A₁ phenotypes ($t_{420}=2.1$, $0.05>P>0.01$).

Table 3 Frequencies of the ABO Phenotypes in Six of the Seven Villages

	n	A ₁	A ₂	O	B	A ₁ B	A ₂ B
Horton	112	0.45	0.03	0.45	0.06	—	0.01
Merton	83	0.35	0.02	0.45	0.11	0.05	0.01
Beckley	100	0.38	0.04	0.46	0.11	0.01	—
Wendlebury	130	0.43	0.08	0.42	0.05	0.01	0.01
Weston	96	0.43	0.03	0.39	0.08	0.04	0.02
Charlton	127	0.45	0.02	0.46	0.07	0.01	—

Although there are significant differences in mean IQ between the seven villages there is no evidence for spatial heterogeneity in the frequencies of the ABO phenotypes (Table 3). The sample can, however, be divided into those who were born in the Otmoor region and those who were born elsewhere and thus compare the frequencies of the ABO phenotypes and their associations with IQ among these geographically migrant and non-migrant groups. For the males, but not for the females, there are significantly fewer O phenotypes among the locally born than there are among those born outside the Otmoor region (Table 4). The males and females not born locally also have significantly higher mean IQs than those who were born locally, regardless of their blood group phenotype. In both the non-local females and the local males the mean IQ of the O phenotypes is higher than the mean IQ of the A₁ phenotypes, but the difference is not significant (Table 5).

Table 4 ABO Phenotypes Among the Locally and Non-locally Born

		A ₁	O	Others	Estimated gene frequency O
Females	local	32	32	5	0.68
	non-local	97	105	36	0.66
$\chi^2_2=2.98$, $P>0.2$					
		A ₁	O	Others	Estimated gene frequency O
Males	local	56	30	13	0.55
	non-local	81	111	30	0.69
$\chi^2_2=12.5$, $0.01>P>0.001$					

There is thus genetic evidence for at least two population groups in the area, but this alone cannot be responsible for the association between ABO blood group and IQ which the analysis reveals. Unfortunately we do not know how typical either the migrants or non-migrants are of the genetic populations they represent. Selective migration could account for the pattern of differences between the sexes and between the locally and non-locally born but only by accepting a direct or indirect association between the ABO blood groups and IQ.

Table 5 Mean IQs of A₁ and O Phenotypes among Locally and Non-locally Born

	n	Females A ₁	n	O	n	Males A ₁	n	O
Locally born	32	99.31 (2.4)*	26	99.96 (2.2)	51	100.53 (2.5)	25	103.44 (1.8)
Non-locally born	97	107.48 (1.2)	106	110.18 (1.1)	83	113.3 (1.6)	114	112.96 (1.1)

* Standard errors given in parentheses.

It is important to stress that our finding of this association between IQ and ABO blood groups in the Otmoor population does not necessarily imply that a similar association will exist in any other population. This will depend on whether the phenomenon is due to linkage disequilibrium or pleiotropy, and true pleiotropies of blood group genes are impossible to identify with the relatively crude characterisation of blood group specificities presently available.

The proportion of the genetic variance for IQ in this sample which is accounted for by this association is small, but it is not to be expected that a single marker locus will be associated with a large proportion of the variance. Thoday⁵ strongly advocated this approach to the analysis of continuous variables in human populations, especially psychometric variables, and our results suggest that the approach is worthwhile.

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Collateral Innervation of Muscle Fibres by Motor Axons of Dystrophic Motor Units

MUSCULAR dystrophy refers to a group of genetic degenerative diseases in which the skeletal muscle fibres undergo a progressive disintegration and are eventually replaced by fat or connective tissue. Besides these degenerative changes resulting in severe atrophy and paresis, the histological study of biopsy specimens also discloses scattered small areas of basophilic sarcoplasm containing increased RNA, and nuclei with prominent nucleoli¹⁻³. The true incidence and functional significance of such signs of attempted muscle fibre regeneration are still uncertain. The electrophysiological data to be presented emphasise that motor axons innervating motor units affected by the disease retain the capacity to successfully innervate additional muscle fibres through collateral sprouts.

Detailed electromyographical studies were performed on seven male patients, aged 7 to 15 yr, with typical X-linked (Duchenne) muscular dystrophy. Standard concentric needle electrodes were used to pick up the potentials of single motor units (the muscle fibres innervated by a single motor axon) during very slight voluntary contraction. The potentials were recorded on magnetic tape and, when played back for detailed analysis, they were made to trigger the cathode ray oscilloscope time base. A delay line in the amplifier input allowed the initial 3 ms before the tripper point on the main potential deflection to be displayed on the oscilloscope screen⁴. Several potentials of the same motor unit can thus be either superimposed on a still photographic film (Fig. 1A-C) or recorded one below the other on a slowly moving film (Fig. 1D). A characteristic motor unit potential recorded in the deltoid of a normal adult volunteer (Fig. 1A) has about 300 μ V peak voltage and its total duration does not exceed about 10.5 ms. In patients with spinal muscular atrophy, many motor axons degenerate and the corresponding muscle fibres undergo neurogenic atrophy; the healthy motor axons present an extensive sprouting of collaterals which reinnervate the neighbouring denervated muscle fibres^{5,6}. In a muscle with such partial neurogenic atrophy the motor unit potentials are of course fewer in number but they present an increased voltage and sometimes also an increased duration^{7,8}. By analysing these motor unit potentials with the method described above, we recently demonstrated another characteristic sign of collateral reinnervation, namely the occurrence of many late components (Fig. 1B) which are delayed by up to about 50 ms with respect to the initial main deflection⁴.

In the affected muscles of patients with X-linked muscular dystrophy, the motor unit potentials are typically reduced both in voltage and duration⁷⁻⁹. We were surprised to find that quite a few of the dystrophic motor unit potentials also present late components (Fig. 1C) because it has generally been held that collateral reinnervation is a feature of neurogenic, but not of myogenic, atrophies. The late components recorded in dystrophic muscles are not an artefact resulting from repeti-

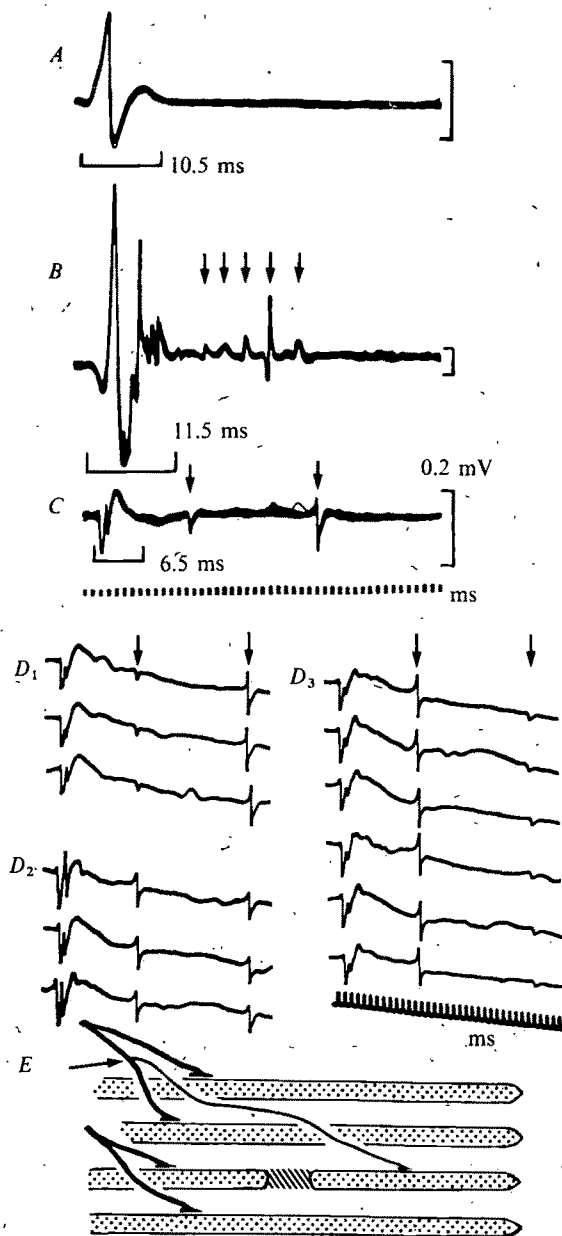


Fig. 1 Motor unit potentials recorded from the deltoid muscle with a concentric needle electrode (Disa model 13K0511) in, A, a normal 35-yr-old male subject; B, in a female patient 12 yr old with spinal muscular atrophy (Wohlfart-Kugelberg-Welander syndrome, juvenile type) since the age of 3; and, C, D, in another male patient 8 yr old with X-linked (Duchenne) muscular dystrophy since the age of 1. The potentials trigger the oscilloscope time-base and are recorded with an ADYU delay line of 3 ms. About seven sweeps are photographically superimposed in A-C. Arrows point to the late components. In D, the motor unit potential of C is displayed on moving film. Notice the changes in wave form when the recording needle is slightly rotated between D_1 - D_2 and D_2 - D_3 . E, Tentative diagram suggesting how a muscle fibre segment isolated by focal necrosis could be innervated by a collateral sprout of a preterminal motor axon (arrow).

tive discharges. They represent muscle fibre activities which are triggered by the action potential of the same motor axon with a longer, but consistent, delay. For example, when the recording concentric needle electrode is slightly rotated in the muscle (Fig. 1 D_1 - D_2 and D_2 - D_3), the size and wave form of the several components of this motor unit can be made to vary independently while their respective latencies remain stable. As expected, the changes in wave form are more important for the two small late components than for the main

motor unit potential when the position of the electrode tip changes slightly with respect to the corresponding muscle fibre(s).

Extensive studies on the proximal and distal muscles of patients at different stages of the disease show that the phenomenon is of rare occurrence or absent for the motor unit potentials of normal configuration in the muscles at a pre-clinical stage, and also for the severely disintegrated motor unit potentials in the muscles with severe atrophy and fibrosis in advanced cases. By contrast, in the moderately affected muscles, many genuine late components are recorded in motor unit potentials which present already definite myopathic changes (polyphasia, reduced voltage and duration).

The motor axon innervating such dystrophic motor units thus retains the capability to produce collateral sprouts forming functional neuromuscular junctions on neighbouring muscle fibres. This observation does not seem to agree with the recent proposal that human dystrophies could result from a primary lesion of the motoneurons¹⁰. This issue is important and we have been careful to limit the present paper to evidence consistently recorded in human patients with genuine X-linked dystrophy, as shown by the clinical features, the marked elevation of serum creatine phosphokinase and the unequivocal electromyographic signs of myopathy in the proximal muscles. It should be pointed out that the evidence for denervation and neurogenic atrophy in Duchenne dystrophy¹¹ is still rather controversial, for it was obtained in a foot muscle (extensor digitorum brevis) which discloses neurogenic changes even in normal young subjects with no neurological disease¹².

Our results raise the question of which muscle fibres become available for accepting the collateral innervation in a dystrophic muscle. One possibility is that muscle fibres would become denervated but remain excitable in these muscles. This possibility should not be excluded but it seems to us rather unlikely; it implies that, in human X-linked dystrophy, the process of progressive disintegration should paradoxically involve the motor axon before the corresponding muscle fibres if the latter were indeed to be made available for accepting innervation by a new axon sprout. The well documented dropping out of muscle fibres from motor unit potentials as the dystrophy progresses indicates rather that the motor axon remains functional until only a few muscle fibres remain excitable in the motor unit. The current interpretation of this fact emphasises that the process of progressive disintegration must involve the muscle fibres before the corresponding motor axon⁷⁻⁹. This concept remains valid even if the primary dystrophy defect proves to be the lack of a trophic factor inadequately supplied by the motoneurone to its axon, which is our preferred form of the neurogenic hypothesis.

If no significant numbers of viable muscle fibres lost their innervation to become able to accept the collateral sprouts, the latter can only innervate newly formed muscle fibres. This raises interesting possibilities because muscle regeneration processes are known to occur in dystrophy¹⁻³. Our suggestion (Fig. 1E) is based on the observation that the dystrophic degeneration sometimes only affects part of the long muscle fibre and that the fibre segment thus disconnected from the endplate zone by the focal necrosis will reform its membrane and even display histological evidence of regenerative activity^{1,13}. Such viable isolated segments thus become new muscle fibres which can be innervated by an axon collateral. The delay of their action potentials with respect to the main motor unit spike would be related, among other things, to the longer conduction distance and the slower velocity in the thin axon collaterals (Fig. 1E, arrow). As well as regeneration of muscle fibre segments isolated by focal necrosis, one must consider both longitudinal splitting of muscle fibres into several daughter fibres and the formation of new fibres from myotubes and satellite cells¹⁴. The relative importance of these various regenerative processes for supplying viable muscle fibres in dystrophic muscles remains to be evaluated.

In any case, as newly formed muscle fibres are known to be

present in dystrophic muscles³ and as genuine processes of collateral innervation have now been disclosed (Fig. 1C and D) it becomes difficult to escape the suggestion that new muscle fibres formed by segmentation, longitudinal splitting and (or) regeneration must become enrolled into existing motor units and activated in voluntary contractions. The contribution of laterally innervated fibres to the mechanical force output of the diseased muscle should be assessed and the nature of the muscle fibres concerned should be examined in further studies. The reparative process of collateral innervation described in this paper is considered likely to delay the onset and progression of the clinical weakness in patients with X-linked muscular dystrophy.

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Preliminary Characterisation of the Caudal Organ Secretion of *Apodemus flavicollis*

THE existence of a secretory organ lying along the proximal third of the undersurface of the tail of the mouse *Apodemus flavicollis* has been known for some time¹. Such organs are present in other species of the same genus^{2,3}. The organ is composed of holocrine sebaceous tissue up to 1 mm deep and produces a thick milky exudant which can sometimes be expressed by gentle lateral pressure on the tail. The organ is anatomically similar to that found in the tails of *Perognathus* and *Chaetodipus*⁴. The function of the organ in *A. flavicollis* is not known¹, but it is possibly involved in olfactory recognition of territory, or self advertisement. It may also be used in mate and nest marking. Its secretion has a characteristic odour to the human nose resembling the odour of voles rather than the odour of laboratory mice. Microscopically, the organ is plainly visible in adult male mice, but much less so, if at all, in both adult females and juveniles of either sex.

A population of *A. flavicollis* inhabiting a *Quercus-Carpinus* forest close to Brno, Czechoslovakia, was studied by

break-back trapping during the summer of 1972. Trapped animals were weighed and their sexual and reproductive conditions determined. Females were recorded as having the vagina perforate (in breeding condition), imperforate (not in breeding condition unless copulation plug present), pregnant and/or lactating. Males were recorded as having testes scrotal (in breeding condition) or abdominal (not in breeding condition). The mean length of the testes was recorded to provide an indication of sexual maturity. These data, from twenty-one specimens, were supplemented by data from a further five specimens caught in Sussex in the autumn of 1972. From each trapped animal the proximal 12 to 15 mm of the skin of the tail was sealed in a small tube with one drop of ultra pure xylol, which acted both as a solvent for the secretion and as a preservative for the tissues.

Before analysis, the tail organ was ground in the tube. Extra xylol was added only if the seal of the tube had allowed some evaporation to occur. The extracts were analysed by gas-liquid chromatography (see legend to Fig. 1).

The tail gland secretion was found to consist of a mixture of twenty-six principal components or component complexes with boiling points ranging from 210° C to 300° C (Fig. 1A). Only one of these components, peak *i*, is present in any amount in the skin of the distal portion of the tail (Fig. 1B). This peak has also been found in chromatograms from skin extracts from the head and neck region of both *A. flavicollis* and the related species, *A. sylvaticus*.

The chemistry of tail organ secretion is the subject of a continuing study and will be reported elsewhere but it is known that peaks *a* to *m* form homologous series of long chain esters of long chain alcohols, with molecular weights of from 396 to 466 (D. M. S., unpublished observation). What is reported here is the amount of difference found in tail organ secretions from different sex and age classes of the population. There is some variation within each age and sex class but this is much less than that between classes. The examples chosen for illustration are completely typical of their represented classes. Adult males are characterised by having many peaks, especially many of high boiling point (Fig. 1A). Adult females have, typically, no peaks of high boiling point and only a small development of the components with low boiling point (Fig. 1C). Female tail secretion is remarkably similar to that of juvenile males (Fig. 1D) and to juvenile females. In essence, the proximal portion of adult female, juvenile female and juvenile male tail is chemically similar to distal tail skin or general skin of adult males.

At what stage in development does the tail organ of the male produce typical male substance? An indication of this may be gained from the state of sexual maturity. The average testis length of adult males in the Brno population in 1972 was 13.85 mm and the average body weight 28.24 g. In every respect (that is, coat colour, tail length and hind foot length) the animal represented in Fig. 1E resembled an adult more than a juvenile. Its chromatogram shows a stronger relative development of components *k*, *l*, *o*, *p*, *r* and *x* than is apparent in Fig. 1D. In the development of components *k*, *l*, *o*, *p*, *r* and *x* and *z*, however, it resembles more an adult male (Fig. 1) than it does an adult female (Fig. 1C).

A further point of interest arises from these observations. A cluster of peaks of boiling point between 150° C and 180° C was observed in all samples analysed. By far the greatest development of these occurs in juvenile mice of both sexes. The same components also occur in adult males but, relative to the rest of the peak pattern, they are in very much smaller amounts. They are practically, but not completely, absent from secretions produced by pregnant and lactating mice. There is some evidence that they occur in perforate (that is, sexually mature) females that are neither pregnant nor lactating.

These observations seem to suggest that the function of the secretion is sociological rather than physiological. By producing a secretion similar to that produced by their mothers, juvenile males are possibly treated as females by adult males

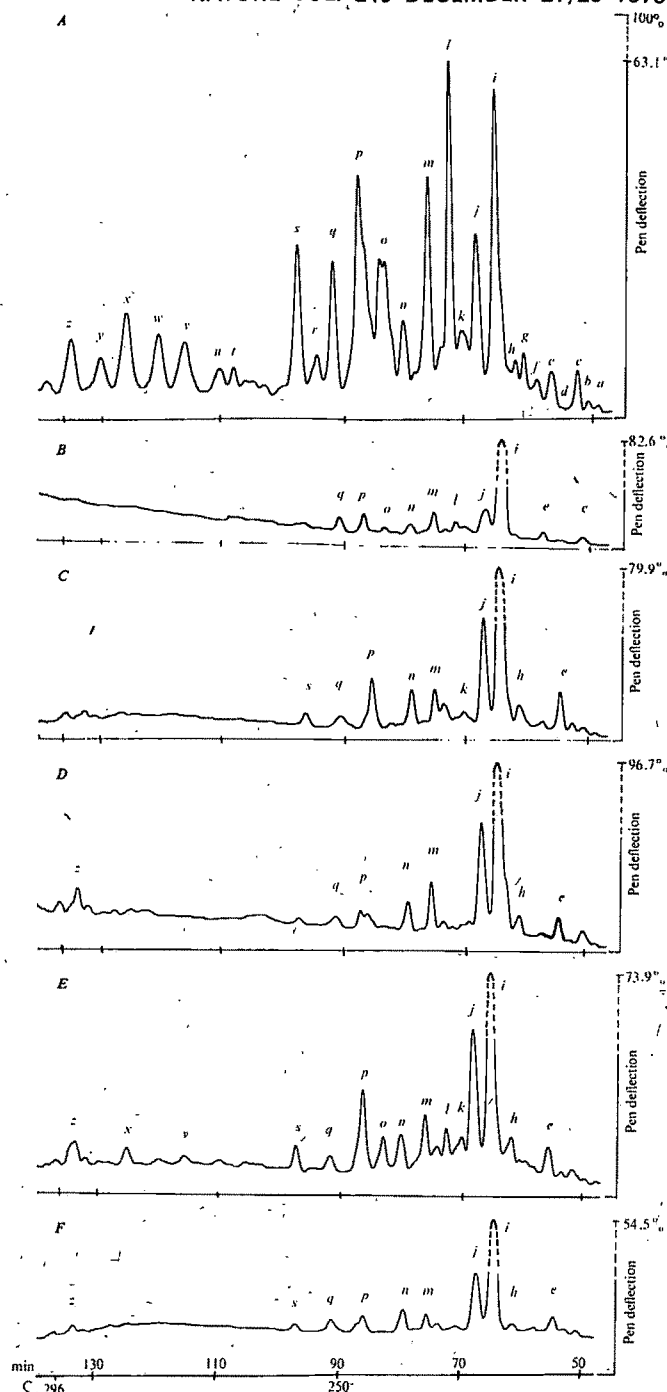


Fig. 1 A, Chromatogram of caudal organ extract of adult male *Apodemus flavicollis* (weight of mouse, 36.8 g; testes scrotal; mean testis length, 14.5 mm). Letters *a* to *z* indicate twenty-six principal components or complexes of components. Sample size 1.5 μ l. Pye Unicam gas-liquid chromatograph series 104, dual heated flame ionisation detectors. Columns: 1.5 m $\times$ 4 mm glass 3% dimethyl silicone gum on 100-120 mesh Diatomite CQ. Carrier; N_2 at 54 ml min^{-1} . Column temperature: 170° C for 5 minutes then 1° C min^{-1} , 296 to ∞ . Detector temperature: 300° C. Injection temperature: 235° C. B, Chromatogram of skin of adult male *A. flavicollis* from the non-glandular (that is, distal) region (weight of mouse, about 35 g; testes scrotal; mean testis length, 14.2 mm). Sample size 3 μ l. (Chromatography details as in A.) C, Chromatogram of caudal organ extract of adult female *A. flavicollis* (weight of mouse: 33.6 g, pregnant, five embryos). Sample size 2 μ l. (Chromatography details as in A.) D, Chromatogram of caudal organ extract of juvenile male *A. flavicollis* (weight of mouse, 16.6 g; testes abdominal; mean testis length, 6.2 mm). Sample size 3 μ l. (Chromatography details as in A.) E, Chromatogram of caudal organ extract of juvenile male *A. flavicollis* (weight of mouse, 19.0 g; testes abdominal/scrotal (?); mean testis length, 8.9 mm). Sample size 1.5 μ l. (Chromatography details as in A.) F, Chromatogram of caudal organ extract of adult female *A. flavicollis* (weight of mouse, 18.1 g; perforate, non-parous). Sample size 3 μ l. (Chromatography details as in A.)

and are not subject to attack. In addition, they produce a juvenile component complex which, probably by virtue of its relative abundance in this age class, may assist in identifying them as juveniles. As soon as they are physiologically capable of competing with the males, they produce a secretion more like that of their father than their mother, although the low-boiling point fraction is still present. If a similar situation exists in other species of rodents, and there is some evidence to suggest it does (D. M. S., unpublished data), then it could help to explain why juvenile male rodents are not attacked by adult males^{5,6}. Further, if the quality of secretion is capable of change in response to hormonal changes resulting from increasing population pressure or onset of breeding, the differential tolerance of males to one another during different phases of a population cycle could be explained^{7,8}. Questions arising from these suggestions are the subject of continuing studies.

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Distribution and Immunology of Mammalian Nerve Growth Factor

We report here a series of experiments in which we have measured the amount of nerve growth factor (NGF) present in the serum of a number of species. We have also compared the immunological properties of the serum NGF with purified NGF from mouse salivary gland and from a snake venom.

'Nerve growth factor' describes that group of proteins which, when injected into neonate animals, produces hyper trophy and hyperplasia of the neurones of the sympathetic nervous system (for leading references, see ref. 1). It also produces characteristic outgrowths of fibres from explanted embryonic chick sensory or sympathetic ganglia; this response forms the basis of an *in vitro* assay method developed by Levi-Montalcini *et al.*². We used a modification³ of this assay. Levi-Montalcini and her coworkers have reported that NGF is a normal component of the sera of all mammals^{4,5}, including man, but the experimental details seem to refer only to mouse serum^{6,7}. In the present study, the direct assay of a number of different sera, either undiluted or at dilutions of up to a hundred-fold, gave essentially negative results. Suboptimal results were observed in some cultures but were below the standard⁴ required to define activity. To improve sensitivity, a fractionation procedure based on the known^{8,9} basic properties of NGF was then used. The sera were concentrated and desalted by pressure dialysis and lyophilised. Batches were reconstituted in a buffer solution containing 2-amino-2-methylpropane-1,3-diol/HCl (0.01 or 0.05 M, pH 8.5), dialysed against the buffer for 18 h, and then chromatographed on OAE A-25 Sephadex equilibrated in the same

conditions. Activity was detected typically in the unabsorbed fractions (~1-5% of the whole protein). The serum of the adult male mouse proved to be an exception: the active material was retained by the resin but could be eluted by application of a higher concentration of starting buffer (0.1 M). It is not clear whether this atypical behaviour reflects a fundamental difference in the nature of the protein from this source, or whether it is indicative of some interaction between the factor and other serum proteins. On the basis of the activities of the individual fractions, the specific activities of the different sera are given in Table 1. The results are the means from several experiments; occasional negative results were obtained, presumably because of the very low levels of NGF in the sera and of the variation from batch to batch. It can be seen that NGF was detected in all the sera examined, the level varying by approximately 200-fold.

Table 1 NGF Activity in Sera

Animal	NGF activity (biological units ml ⁻¹)
Mouse ♂	10-20
Mouse ♀	0.7
Human	1.5
Pig	0.2-0.4
Horse	0.1-0.5
Foetal calf	0.1-0.2
Cockerel	0.2

The level of NGF in male mouse serum deserves special comment. A specific activity of 10-20 biological units ml⁻¹ was obtained for this material, a level which should have been detected easily by direct assay of the whole serum after appropriate dilution. Our failure to do so may mean that whole serum contains an inhibitor which is removed on fractionation. The active fractions from the male mouse and from human serum were further fractionated by gel filtration on Sephadex G-100. In each case, active material was eluted in a fraction containing 5-15% of the applied sample and with an apparent molecular weight in the range 10,000-70,000. These fractions were used in the experiments with antisera described below.

Nerve growth factor can be isolated from mouse submaxillary gland in two forms: (1) a high molecular weight aggregate (7S NGF) (ref. 10) containing NGF and two other inactive proteins and (2) as an active homogeneous entity (β subunit, 2.5S NGF) containing two identical polypeptide chains¹¹⁻¹³. The β subunit has a molecular weight of about 30,000 and contains no carbohydrate⁸. Snake venoms also contain NGF, and that from *Vipera russelli* has been shown to be a glycoprotein containing 20% carbohydrate and with a molecular weight of about 37,000 (ref. 9). The non-carbohydrate part is about the same size as the dimeric β subunit and the two have comparable specific activities *in vitro* but the degree of structural homology, if any, is unknown.

Antisera to both forms of mouse salivary gland NGF (7S and β subunit) and to the NGF from the venom of *Vipera russelli* were raised in rabbits in conventional manner. Using successive two-fold dilutions, the highest dilution of antiserum required to block the activity *in vitro* of one biological unit of NGF was determined for all the possible combinations of antigen and antibody (Table 2). It can be seen that the two forms of NGF from mouse salivary gland are very similar antigenically but are quite different from the NGF from the venom of *Vipera russelli*. The biological activity of the mouse antigen is either unaffected or blocked only by very high concentrations of the antibody to the snake antigen and *vice versa*. This is not surprising as, although the proteins have similar biological effects, the degree of homology between the active polypeptide chains of the NGF from the two species

is unknown and, further, the antigen from the snake is a glycoprotein whereas that from the mouse is not. The carbohydrate components of glycoprotein antigens are known to be capable of contributing to or determining the immunological properties of the molecule¹⁴. What is surprising, however, is that the NGF present in the serum of mouse and of man is, in terms of the test described above, practically indistinguishable from the snake venom NGF and not at all like the NGF present in mouse salivary gland. The precise significance of these findings is not clear. The NGF in mouse serum detected by our procedure cannot be exactly the same as the NGF in the salivary gland and it is tempting to suggest that the serum factor may be a glycoprotein in the same way as the venom NGF. The similar immunological properties of the molecules could then arise from common carbohydrate determinants. A number of workers have suggested, however, that the NGF in mouse serum may be derived chiefly from the submaxillary gland^{7,15}. If the serum protein is actively synthesised in the gland, it must be modified on secretion such that its antigenic properties become altered. A modification of this type could be introduced if carbohydrate is attached to the newly synthesised protein to promote its transport into the extracellular environment. Such a general role for the carbohydrate moieties of glycoproteins has been suggested by Eylar¹⁶, to account for the observation that the majority of extracellular proteins, and especially serum proteins, contain carbohydrate. Consistently with other reports^{17,18}, however, we have failed to detect active material in the submaxillary glands of other mammalian species and the most reasonable interpretation of the present results is that the NGF detected in the serum of all the species tested (including mouse) does not arise from the submaxillary gland but is synthesised elsewhere.

Table 2 Immunological Properties of NGF

Antigen	Antibody titres—reciprocal dilution blocking the activity of 1 BU		
	MSG 7S	Antibody MSG β subunit	<i>Vipera russelli</i>
MSG 7S	3,000–6,000	6,000	0–15
MSG β subunit	6,000	6,000	≤ 3
<i>Vipera russelli</i>	≤ 3	≤ 3	1,500–3,000
Human serum	0–6	15	1,500
Mouse serum	0–6	≤ 3	1,500–3,000

The value obtained in the present experiments for the NGF content of the serum of the male mouse (10–20 units ml⁻¹) should be compared with the values of 15 units ml⁻¹ and 180 units ml⁻¹ reported by Hendry¹⁵ and by Johnson *et al.*¹⁹, using radio-immunological methods based on mouse salivary gland NGF. That any measure of agreement should exist at all demands some comment. The radio-immunoassay procedure requires that the NGF in the serum should be recognised and bound to the antiserum prepared against the NGF from mouse salivary gland, whereas the present findings show that the biological activity of serum NGF is hardly affected by this particular antiserum. It is, of course, true that combination of antigen and antibody does not necessarily lead to loss of the antigen's specific biological activity^{20,21}. Whether this applies in the present case can, however, only be settled by careful immunological and biological testing on the same samples.

It is also possible that mouse serum contains more than one form of NGF and that in our procedure only one form is isolated. This is conceivable as it has been suggested recently that NGF is not produced in any specific organ in the animal but is synthesised in a variety of different tissues⁵. The proteins produced in this way may not have precisely the same immunological properties. In

any event, the findings suggest that the biological significance of the form of NGF present in mouse submaxillary gland is open to question.

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Electrophysiological Evidence for Existence of Neurones sensitive to Direction of Depth Movement

RECENT psychophysical evidence suggests that there are movement detectors in the human visual pathway selectively sensitive to different directions of motion in three-dimensional space¹⁻⁵. In animals (such as the cat) there are single nerve cells with properties which suggest that they signal when an object is moving in depth away from the plane of binocular fixation⁶.

Regan and Spekreijse^{7,8} report of electrical signals generated by the human brain and specific to changes in retinal

disparity (that is, to stimuli which appeared to move in depth) suggested the possibility of establishing a stepping-stone between subjective studies of human depth perception and the properties of disparity-sensitive single neurones in animal brains. We have recorded electrical brain responses in man, and report here evidence for the existence of neurones that respond differently to stimuli that move away from and towards the plane of binocular fixation.

The left and right eyes viewed a 5° pattern of randomly-arranged black dots that differed in only one respect. This was that the central 2° of the left eye's pattern could be moved from side to side. When the left eye alone was used, the subject saw the central 2° move from side to side (monocular condition). When the two patterns were viewed by both eyes in binocular fusion, however, the movement produced a compelling illusion that the central 2° of the pattern was moving backwards and forwards in depth (stereoscopic condition)⁸⁻¹¹. (The stimulus did not really move in depth at any time. All depth changes were illusions produced by changing retinal disparity. For brevity, however, the phrases 'depth changes' and 'position in depth' will be used in referring to these illusions.) The initial displacement in depth of the 2° target could be set so that it appeared to be located in space either in front of or behind the plane of binocular fixation. Ocular convergence was monitored by means of nonious lines. These enabled a change in angular convergence of 0.5 arc min to be detected (much smaller than the disparity change required to elicit an appreciable evoked potential (EP)).

In some experiments a bar stimulus was used. The left and right eyes viewed identical patterns of randomly-arranged 2 mm dots. These patterns defined the fixation plane. A black bar that subtended 2° × 8' was located 1° to the right of the central nonious lines. The left eye's retinal image of this bar could be moved from side to side.

Chlorided silver disks were attached to the occipital scalp (1 cm above the inion) and to the left mastoid. Electrical brain responses (EPs) were recorded between these electrodes by means of an averaging computer⁸. The right mastoid was grounded. The bandpass of the recording system was 0.08 Hz to 40 Hz (3 dB down). Reducing the high frequency cut from 40 Hz to 12 Hz did not, however, appreciably change our amplitude measures but did reduce noise, so this bandpass was used to record the waveforms of Fig. 1.

A prominent, positive-going wave followed by a negative-going wave was generated for each movement of the stimulus. For both directions of stimulus movement and for both stereo and mono conditions, the latency to the peak of the positive-going wave was roughly 120 ms and the latency to the peak of the negative-going wave was roughly 220 ms.

These responses are similar to those observed by Regan and Spekreijse except that they did not observe such large negative-going waves⁷. When we used Julesz patterns similar to those used by Regan and Spekreijse, however, the negative-going wave was much less prominent.

Figure 1A shows that stereoscopic (stereo) stimulation gave quite different responses to those elicited by monocular (mono) stimulation. The upper two records in Fig. 1A show the brain's electrical responses to a target that appeared to move abruptly backwards and forwards in depth at a rate of 0.9 Hz (stereo condition). The target remained in front of the fixation point in one recording and behind the fixation point in the other recording. It is clear that for a target located in front of the fixation plane, quite different response amplitudes were recorded for movements directed towards and away from the eye. For stimuli located behind the fixation point the two directions of movement also gave different responses; in this case, however, response amplitudes were roughly similar and the difference was one of waveform. The two lower traces of Fig. 1A show that these directional asymmetries disappeared when the retinal image movements were not accompanied by changes in retinal disparity (mono

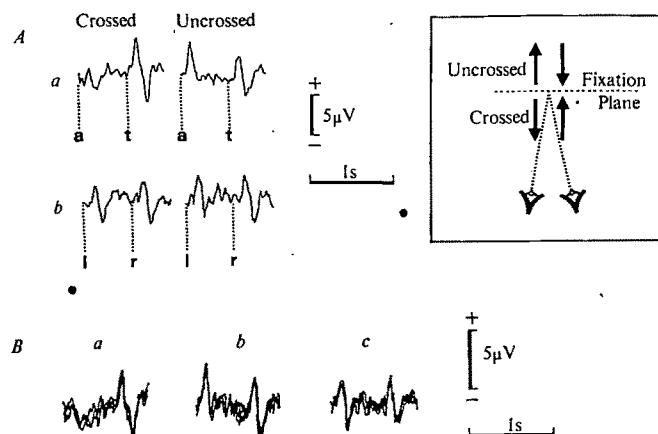


Fig. 1 A, Electrical brain responses (a) to stereo movements for targets located in front of and behind the plane of binocular fixation and (b) responses to monocular control stimuli similarly located in front of and behind the fixation plane. Insert illustrates the apparent positions and directions of movement in space in the two stereo conditions. B, Variability illustrated by three superposed traces for, a, stereo crossed; b, stereo uncrossed; and c, mono stimulation. In the stereo traces t means movement towards the eyes and a means movement away from the eyes. In the mono traces l and r refer to leftward and rightward movements respectively. Each trace is the average of 500 sweeps in A and 100 sweeps in B. The stimulus frequency was 0.9 Hz and the sweep duration 1 s. The stimulus target was a 2° circle of random black dots surrounded by an annulus of similar dots extending to 5°. The dots occupied some 1% of the total area. Mean stimulus luminance 110 cd m⁻². Distance from eye to target 75 cm. The stimulus displacement of 10' was the same in each condition.

condition). This finding also held when, in the mono condition, the right eye viewed an uncorrelated random dot pattern. It is important to note that: (a) in both stereo and mono conditions the left eye only received movement stimulation, and (b) these movements were identical in the mono and stereo conditions. In the stereo situation the right eye viewed a similar but static pattern, so that the brain could compute changes in retinal disparity (and thus the target appeared to move in depth), whereas in the mono situation the right eye was occluded so that the brain could compute only changes in retinal image position (so that sideways movements only were seen).

Figure 2 illustrates a second distinction between stereo and mono responses, and shows the effect of changing movement amplitude in the four stereo (a-d) and two mono control (e, f) situations. In the mono situation, response amplitude showed no further increase when stimulus amplitude was progressively increased beyond 5 arc min. In contrast, responses to stereo stimulation either grew progressively as stimulus amplitude increased, or did not saturate until stimulus amplitude exceeded 15 arc min. Thus, the relationships between response amplitude and stimulus excursion were quite different in the mono and stereo situations.

These results (Figs 1 and 2) held for each of a total of fifteen separate experiments.

A further point is that the data of Fig. 1A cannot be explained simply by assuming that different responses are elicited by movements in depth directed towards and away from the eyes. Figure 2 provides additional evidence that this explanation is insufficient. Independently of whether the target was in front of or behind the fixation point, movements directed away from the fixation point gave concave downwards curves (Fig. 2a, d) whereas movements directed towards the fixation point gave concave upwards curves (Fig. 2b, c). It is worth noting that from this it follows that differences in absolute amplitudes between the various types of stereo and mono responses must be considered in relation to stimulus amplitude (compare with Fig. 1).

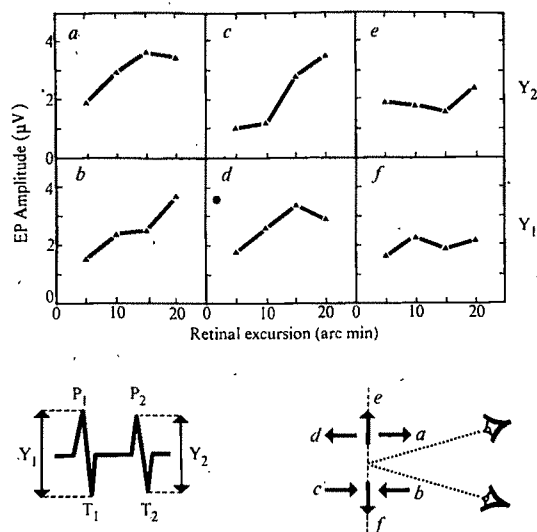


Fig. 2 Effect of stimulus amplitude on the electrical response of the brain. Each curve is a plot of response amplitude in microvolts (μV) against the excursion of the left eye's target in arc min. *a, b*, Stereo crossed; *c, d*, stereo uncrossed; *e, f*, monocular stimulation. One insert shows how response amplitude was measured for targets moving towards the eyes (Y_2) and away from the eyes (Y_1) (see ref. 8, page 229, for a discussion of this definition of response amplitude). The other insert illustrates the target position and direction of movement for each of the four stereo and two mono plots. The measurements were derived from averages of 100 sweeps, each of 1 s duration. The stimulus was a vertical $2^\circ \times 8'$ black bar located 1° to the right of the nonious lines. The fixation plane was defined by a 5° square pattern of random black dots that occupied roughly 1% of the area of the 110 cd m^{-2} background. Distance from eye to target was 75 cm.

Our conclusions hold for both bar and dot patterns, though there were some waveform differences. Although bar patterns gave smaller responses than dot patterns, the differences between stereo and mono conditions seemed clearer for bar patterns.

The findings of Figs 1 and 2 can be explained on the basis of the two following assumptions: (a) The way in which the brain handles information that a target's retinal disparity has changed depends on whether the target's mean disparity is crossed (that is, target in front of the fixation point) or uncrossed (target behind the fixation point). (b) Information of a change in retinal disparity is handled differently when the target is moving away from the fixation point than when it is moving towards the fixation point.

Assumption (a) would agree with psychophysical evidence for the existence of the disparity pools postulated by Richards¹²⁻¹⁵. Assumption (b) would agree with reports of psychophysical adaptation to the direction of movement in three-dimensional space¹⁻⁴. The distinction reported here between human brain responses to depth movements directed away from and towards the fixation point may reflect the activities of neurones selectively responsive to the movement of a target whose disparity is changing. Though they seem rare, such neurones have been found in cat by Pettigrew⁶ and in monkey by Zeki (personal communication). Further, the neurones reported by Pettigrew were selectively sensitive to disparity changes relative to the point of fixation (directed away from the point) which would agree with our data of Fig. 2.

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Experimental Creation of Unusual Neuronal Properties in Visual Cortex of Kitten

A NORMAL cat faces the visual world with an arsenal of feature-detecting neurones in its visual cortex. Virtually every cell is selectively sensitive to the orientation of an edge moving across its receptive field¹ and the whole gamut of possible orientations is represented among the complete population of neurones.

Undoubtedly visual experience itself, early in the kitten's life, plays at least some part in setting up these orientation-detecting neurones. The visually inexperienced kitten's cortex has large numbers of cells that are non-oriented (responding weakly to edges of any orientation) and even some that are totally unresponsive to visual stimuli^{2,3}. Indeed, kittens reared in restricted visual environments, consisting of edges of one orientation, fail to develop cortical cells responding optimally to contours of the orthogonal orientation^{4,5}, even if the exposure is remarkably brief⁶.

During a series of experiments to determine the exact kind of visual stimulation needed to produce the full complement of normal orientation-selective cortical neurones, we reared two kittens in such a manner that almost their entire visual experience was restricted to an array of coarsely-spaced white spots on a dark background. Our rearing procedure was very similar to that of Blakemore and Cooper⁵. Each kitten was housed in a darkroom from the time of eye opening and exposed to a spot pattern for about 2 h each day. The kitten was placed in a transparent cylindrical chamber suspended in the centre of a larger cylinder, on the inside walls of which the spots were displayed. With the kitten looking straight ahead the maximum and minimum viewing distances were restricted to about 8 cm and 32 cm respectively. If it looked far up or down the walls of the display cylinder the maximum viewing distance increased to about 55 cm.

For Kitten 1 the white spots were 0.5 cm in diameter, subtending a visual angle of about 1° to 3.5° for straight ahead viewing. The spots were irregularly scattered over the dark background with a minimum spot separation (centre-to-centre) of 4 cm (7° to 23°) and an average separation of about 7 cm (12° to 41°). For Kitten 2 the spots were 1.3 cm (2.5° to 9°) in diameter with roughly the same spacing. Kitten 1 had 80 h of this visual experience from 3-10 weeks of age, Kitten 2 had 52 h from 3-8 weeks.

Immediately after the period of restricted rearing, we used conventional methods to record activity from single neurones in the visual cortex. The kittens were paralysed with Flaxedil ($7.5 \text{ mg kg}^{-1} \text{ h}^{-1}$) and anaesthetised with 75% nitrous oxide. The responses of the neurones were studied by back-projecting spots, bars, edges and so forth, on a tangent screen 57 cm in front of the eyes.

Histological reconstruction showed that the penetrations were made in area 17, in the area centralis projection area. The microelectrode was purposely driven down the medial

bank of the postlateral gyrus to ensure that it sampled from a wide region of cortex, crossing the borders of many cortical columns¹. In both cases the electrode penetration was more than 3 mm in depth. As in previous experiments on kittens reared in restricted environments^{5,6}, we found no large regions of silent cortex that might have indicated massive degenerative changes. All receptive fields were within 10° of the area centralis and most were within 5°. There were no obvious differences between the two animals in average receptive field size, which was comparable to that for similar samples from adult cats.

Using line stimuli, we were able to classify all neurones into one of the five categories found in normal and visually inexperienced kittens. (1) Orientation-selective: having a clear preferred orientation for moving bars, with no response at all to a bar of the orthogonal orientation. (2) Orientational bias: having an obvious preference for one orientation, but responding somewhat to all. (3) Non-oriented: firing equally for all orientations. (4) Pure direction-selective: firing to any stimulus moving in a preferred direction but with no response in the reverse direction. (5) Visually unresponsive: with spontaneous activity but no response to our repertoire of visual stimuli.

One feature of these cortical neurones was, however, most unusual. A large proportion of the visually responsive cells discharged just as vigorously, if not more so, to moving spots of roughly the angular size experienced during rearing as to extended contours. Thus many non-oriented cells had a preference for spots (rather than long lines) moving in any direction: Fig. 1*a* shows responses from such a cell (recorded from Kitten 1), which preferred a spot of about 2° in diameter. The pure direction-selective cells also responded vigorously for spots moving in the preferred direction (Fig. 1*b*) and most cells, classified as orientation-selective or orientational bias on the basis of their responses to long lines, responded at least as well to a small spot moving along the correct axis as to an optimally oriented line (Fig. 1*c*).

The results are summarised in Table 1, which shows the total number of units of each type and the number of cells responding at least as well to spots of the appropriate size as to long lines. A large proportion of the visually responsive cells (88% in Kitten 1, 89% in Kitten 2) had this unusual property.

These results cannot be attributed to the young age of the kittens, since a control animal (Kitten 3), reared in a normally illuminated laboratory environment and recorded from only 5.5 weeks of age, had an essentially adult visual cortex (Table 1). Almost every cell was clearly orientation-selective and only 16% responded equally well to 1°–5° diameter spots as to elongated bars. Nor can the observations be explained by the period of dark rearing until 3 weeks the unusual regime of visual stimulation: in a second control animal (Kitten 4), which was treated identically but reared in an environment of vertical stripes⁵ for a total of 49 h from 3–7 weeks, only

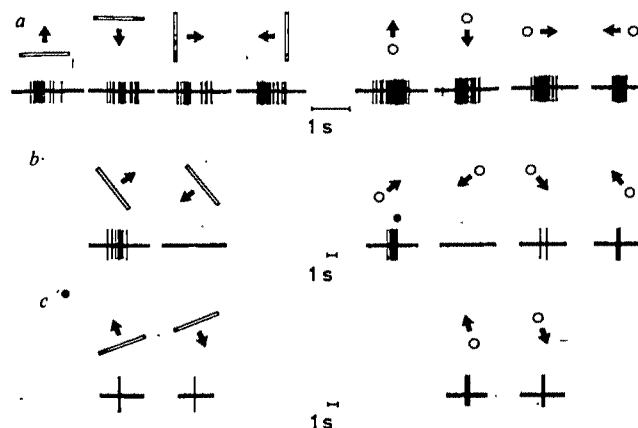


Fig. 1 Oscilloscope records of responses from three cortical neurones recorded in Kitten 1. The stimulus and its direction of movement across the receptive field are shown above each record: a long white bar (approximately $20^\circ \times 0.25^\circ$) was used for the responses shown on the left, and a 2° diameter white spot for those on the right. *a*, Unit K103-R14: a non-oriented cell. *b*, Unit K103-R38: a pure direction-selective cell. *c*, Unit K103-R12: an orientational bias cell, which preferred the orientation shown, but also gave some response to the orthogonal orientation.

13% of neurones responded equally or better to a small spot as to a bar (Table 1).

In the normal adult cat's cortex there is one class of orientation-selective neurone that prefers edges of a limited length and has little or no response to an extended border. These hypercomplex cells⁷, which are rather rare in area 17, usually therefore respond much better to a spot of a particular diameter than to a long edge. We tested all orientation-selective cells in the experimental kittens with lines of various lengths and not surprisingly most of the cells that actually discharged much more strongly for a spot than a bar also demonstrated length selectivity for bars, typical of hypercomplex cells. Many cells were, however, not of this extreme type: they simply responded just as well to a spot, much smaller than the total length of the receptive field, as to a bar that filled it. The characteristic is almost never seen in the normal adult cat's cortex.

In conclusion, early visual experience of extended straight edges seems to be a principal requirement for the establishment or maintenance of a totally normal visual cortex. Significantly, Kitten 2, exposed to large diameter spots with edges approximating to an extended contour, had many more orientation-selective cells (52% of all neurones) and fewer non-oriented units (14%) than Kitten 1 (23% and 33% respectively), which saw only small diameter spots and therefore very restricted contours. The two control animals (Kittens 3 and 4) both experienced extended contours in their environments and virtually all the neurones sampled from them were orientation selective (93% and 100% respectively). We shall consider

Table 1 Classification of Cortical Neurones Recorded from Two Kittens Exposed to Spots During Development, and from Two Control Animals

	Visually responsive neurones				Total	Visually unresponsive	Overall total
	Orientation-selective	Orientational bias	Non-oriented	Pure direction-selective			
Kitten 1 (small spots)	9 (6)	9 (8)	13 (13)	2 (2)	33 (29)	6	39
Kitten 2 (large spots)	22 (19)	6 (6)	6 (5)	2 (2)	36 (32)	6	42
Controls							
Kitten 3 (normal vision)	29 (3)	1 (1)	0	1 (1)	31 (5)	0	31
Kitten 4 (vertical stripes)	24 (3)	0	0	0	24 (3)	0	24

Numbers in parentheses refer to the number of cells in each category responding at least as well to spots of the appropriate size as to

this question of the relationship between the proportion of orientation-selective cells and the type of visual experience more fully in a future paper.

Prolonged exposure to edges of a particular curvature seems to create neurones that exhibit a preference for just such stimuli. Thus cells in the developing visual cortex seem to have a degree of 'adaptive' plasticity—an ability to match their properties to an unusual visual environment—that normally they would rarely be called on to employ.

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Optical Recording of Impulses in Individual Neurones of an Invertebrate Central Nervous System

FOR many purposes it would be a great advantage if one could measure the activity of individual neurones without the use of an electrode. Since the discovery of changes in the optical properties of axons that occur during the action potential^{1,2}, it has been possible, in principle, to accomplish this using optical techniques. Recently, this was achieved in a giant axon using a merocyanine dye; in a stained axon a single action potential gave rise to a fluorescence increase which was detectable with a signal-to-noise ratio greater than 10 : 1 (ref. 3). Because the membrane area observed in the giant axon experiments was about 10^3 times larger than that of a 50 μm cell body, it was by no means evident that this fluorescent probe would be sensitive enough to monitor electrical activity in smaller cells. Happily, it is; with the merocyanine dye, we are able to detect action potentials in individual sensory neurones of leech segmental ganglia. We hope that this technique can be developed into a powerful tool for studying the functional organisation of populations of neurones.

The leech segmental ganglion (See ref. 4, Fig. 2) seemed a favourable preparation because the ganglion is transparent and its cells are arrayed in a highly stereotyped manner in a monolayer cortex. In addition, many of the cells have been functionally identified. Ganglia from *Hirudo medicinalis* were incubated for 20 min in a Ringer solution^{3,4} which contained a merocyanine dye in a concentration of 0.05 mg ml⁻¹ together with 0.02% Pluronic F-127 (a non-ionic surfactant polyol). The dye mixture was then replaced by a leech Ringer⁴ containing an increased calcium concentration (5 mM instead of 1.8 mM). In this solution the resting and action potentials of leech neurones are maintained with enhanced stability. To reduce photodynamic damage^{5,6} to the cells, the bathing fluid was bubbled with nitrogen, but, despite this precaution, the photodynamic effect associated with this dye limited the duration of the experiments. One of the sensory neurones⁴ was

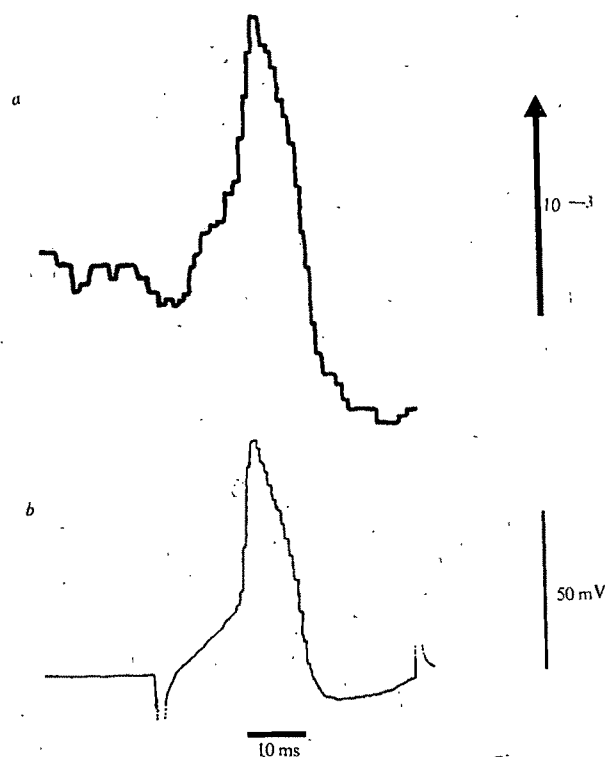


Fig. 1 Simultaneous measurement of fluorescence intensity (a) and membrane potential (b) in a nociceptive (N) cell of a leech segmental ganglion. In this single sweep there was an obvious fluorescence increase during the action potential. The vertical arrow to the right of the intensity trace in each figure represents the stated value of the change in intensity, ΔI , divided by the resting intensity, I_r , in a single sweep. The merocyanine dye was 5-[(3-sulphopropyl-2(3H)-benzoxazolyliidene)-2-butenylidene]-1,3-dibutyl-2-thiobarbituric acid, and is available from Eastman Kodak Co. as 'merocyanine'. The response time constant of the light recording system was 2.2 ms. The signal averager used for recording sampled once every 0.5 ms and this accounts for the jagged character of the records. Cell body diameter, 68 μm . Temperature, 21° C.

impaled with a microelectrode filled with 4 M potassium acetate (resistance 40 to 100 M Ω) and connected to an electrometer (WPI, M-4) which permitted simultaneous stimulation and potential measurement. Light from a Hanovia xenon arc lamp (448C1 or 901C11) was collimated, passed through an interference filter (540 ± 15 nm), and then focused on the ganglion by means of the brightfield condenser on a Leitz Ortholux II microscope. The light collected by a $\times 20$ (numerical aperture 0.4) long-working-distance objective was passed through a Schott OG 590 filter, which attenuated the incident light (by 10^4) and transmitted the emitted light. A pinhole 1.9 mm in diameter was placed in the objective image plane so that the input to the photodetector (EG&G, PV100A) was restricted to light emanating from a region of the ganglion 95 μm in diameter. This pinhole was mechanically positioned over the image of the stimulated cell. The amplified outputs of the photodetector and microelectrode electrometer were fed into separate inputs of a signal averager for storage or averaging.

Figure 1 illustrates the simultaneous measurement of fluorescence (a) and potential (b), recorded in a single sweep from a sensory neurone that responded to noxious stimulation of the skin (N cell⁴). Although there was a slow downward drift in the optical record, the fluorescence increase during the action potential was readily apparent, constituting an effective optical representation of action potentials in this cell. Optical recordings were obtained, as well, in other sensory cells (corresponding to the modalities of touch and pressure) in which the impulses fully invaded the soma. The relative intensity change in the experiments on leech neurones was approximately the same as that found with squid axons ($\Delta I/I \sim 10^{-3}$).

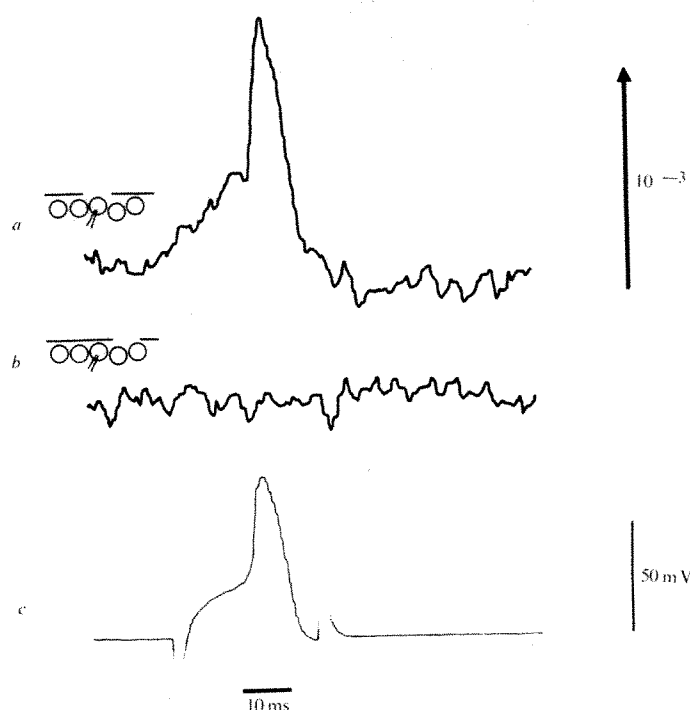


Fig. 2 Measurement of fluorescence intensity (*a*) when the pinhole in the objective image plane was over the image of the stimulated cell, and (*b*) over nearby cells. When the pinhole was moved the equivalent of 95 μm on the ganglion, no intensity change was measured, indicating that the light from the stimulated cell was not significantly spread in the objective image plane. The measurement recorded in trace *b* was made before the measurement recorded in trace *a*. Eight sweeps were averaged in each. The response time constant of the light measuring system was 1.6 ms. Nociceptive cell, 50 μm in diameter. Temperature, 21°C.

suggesting that the merocyanine dye might also be useful as a probe of potential in excitable cells from other species.

Two control experiments ruled out possible artefacts. In the first, the incident illumination was restricted to wavelengths longer than 640 nm, which are not absorbed by the dye. As expected, no intensity change could be detected with this red incident light, while light of the appropriate wavelength (540 nm) resulted in an obvious signal. This demonstrated that the observed effect was a fluorescence change and not, for example, a light scattering phenomenon¹. This result also eliminated the possibility of an artefact resulting from electrical coupling between the systems measuring light intensity and potential. It was also important to show that the light from adjacent cells was satisfactorily separated in the objective image plane, that is, that light reaching the photodetector derived mainly from the stimulated cell, rather than its neighbours in the ganglion. In the experiment shown in Fig. 2, fluorescence was measured (*a*) when the pinhole in the objective image plane was over the image of the stimulated cell, and (*b*) when the pinhole was moved the equivalent of 95 μm in the object plane. There was an optical signal only when the pinhole was positioned over the active cell, indicating that the signal from an individual cell was localised at the cell's image, and was not detectable in adjacent regions of the image plane.

The experiments illustrated in Figs 1 and 2 demonstrate the feasibility of optical monitoring of neuronal activity in one cell with one photodetector. We expect that it will be possible to expand the system to employ an array of detectors so that many neurones can be studied simultaneously. The ability to record activity in many cells at once would allow the construction of a detailed map of the functional connections within a ganglion, and, with additional experiments, should enhance our understanding of the neuronal basis of behaviour.

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Reconstruction of Images from Transforms by an Optical Method

THE holographic reconstruction of the amplitude and phase maps for a bovine liver catalase crystal, by using computer analysis of the image and diffraction pattern obtained in an electron microscope, was reported recently¹. This method used a random number generator to generate an arbitrary phase distribution, and hence to produce from the electron transform a 'first fit' image. This was then filtered by convolution with the image obtained in the electron microscope. We have been attempting to reconstruct images from transforms by an analogue method, using a Rank Precision Industries Image Analyser 3000 to process the images rather than a digital computer. The method which we have defined uses a random spatial frequency generator to produce a 'first fit' image which can be further improved by filtering in reciprocal space. As only the original transform has been used in reconstruction of the image, a task in optics that hitherto has been considered impossible seems to have been achieved (compare Gerchberg¹, where the digital procedure used for reconstruction from the transform, although it used both a transform and an image, worked even when a 'blank' image was supplied).

The use of spatial filtering techniques in optical diffractometry is well known, and is frequently used to improve the signal to noise ratio of micrographs that contain periodic structures. When spatially filtering, the amplitudes of the various components of the Fourier transform of the specimens are modified so that upon recombination, periodic structures in the image are enhanced. If the amplitude filter (spatial filter) placed in the transform plane of the diffractometer is an inverse of the transform of the specimen being examined, then an image will be reconstructed from a 'white' spectrum of frequencies if the phase distribution can be specified.

The phase of the wavefront reaching the transform plane is dependent upon both the physical dimensions of the diffractometer used and the distribution of intensities in the specimen being examined. An attempt was made to synthesise an approximated wavefront at the transform

specimen from which the spatial filter had been obtained (in the same diffractometer).

Assuming that the specimen being examined is optically flat (precautions of this nature are usually taken²), then to a first approximation the phase distribution in the transform plane should be a function only of the diffractometer, for a specimen which is small in comparison with the camera length. If the specimen being examined in the diffractometer is a random frequency generator, then a phase distribution of the desired type could be produced.

The construction of a suitable random frequency generator presents a number of problems, and in practice an optical spectrophotometer cell containing a colloidal dispersion was used. Experiments were carried out using this random frequency generator in the specimen plane of the diffractometer to illuminate spatial filters in the transform plane: the light passing through the spatial filter was recombined and examined for periodic structure and it was found that an approximation to the images from which the spatial filter had been obtained appeared (Figs 1 and 2).

These 'first fit' images that were reconstructed from the spatial filters were then positioned in the specimen plane of the diffractometer and spatially filtered using the same filter from which each image was reconstructed. This spatial filtering improves the image quality and reduces the effect of any faults in the random frequency generator. The use

of spatial filtering to improve image quality could in principle be used numerous times. In practice, however, it was found that the necessary processing began to degrade the image after one cycle of the filtering process and no better quality was obtained.

Figure 1*a* shows the original specimen and Fig. 1*b* its optical transform. The halation from the d.c. spot was reduced photographically before the transform was used in conjunction with the random frequency generator to reconstruct the image. Fig. 2*a* shows the reconstructed image and Fig. 2*b* is its transform.

Experiments were carried out to prove that the reconstruction was not caused by a holographic effect³. This was achieved by blocking out the undiffracted light (which could act as a reference beam) at the transform plane of the diffractometer before it reached the spatial filter being used for reconstruction. Figure 3*a* shows the image produced by this method. Examination of its transform indicates that high order information is not reconstructed as effectively as with the d.c. spot present. The image produced by this method is, however, clearly recognisable, and it can be improved considerably by further spatial filtering; Figs 4*a* and 4*b* show poor quality image improved by this method.

Further work is being carried out to improve the quality of the random frequency generator and the techniques of repeatedly spatially filtering the reconstructed image.

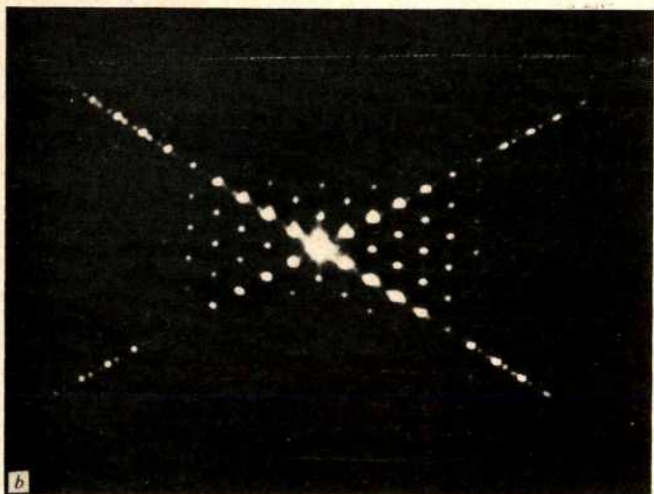
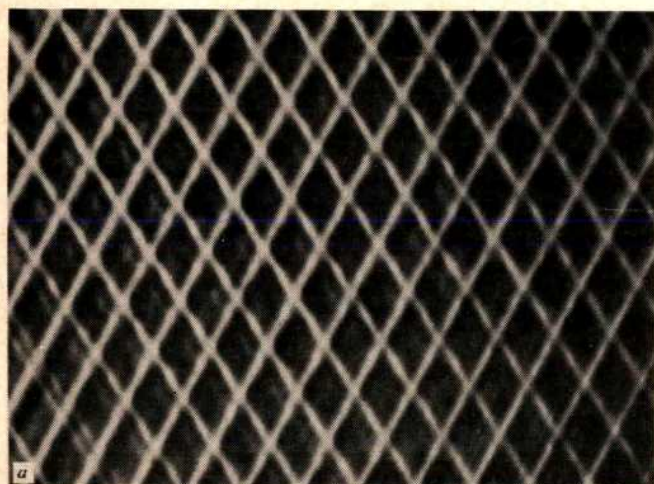


Fig. 1 *a*, The original specimen used in reconstruction experiments, photographed after spatial filtering through the complement of its optical transform. This image is, therefore, the image which would be obtained if a perfect reconstruction, limited only by the quality of the spatial filter, were to be achieved. *b*, Optical transform of the original specimen.

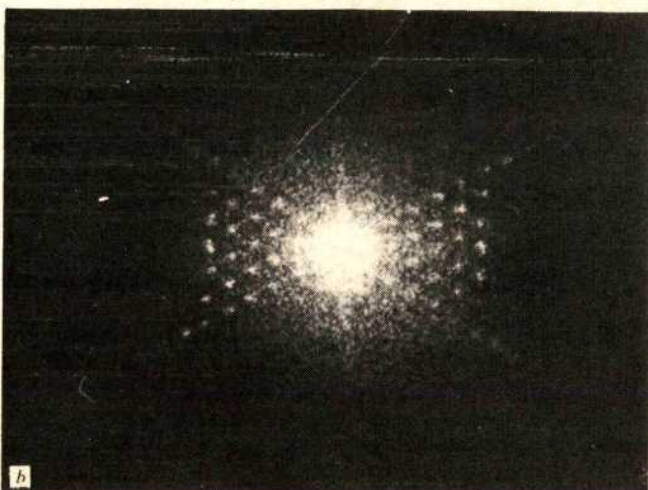


Fig. 2 *a*, A 'first-fit' reconstructed image produced by the procedure defined in the text. *b*, Optical transform of the 'first-fit' reconstructed image. Comparison with Fig. 1*b* indicates a very close relationship, with the strengthening of the d.c. spot and low frequencies indicating a degree of improvement.

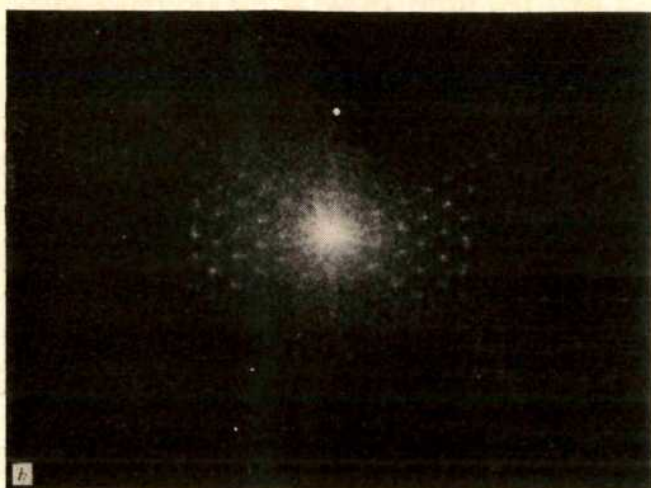
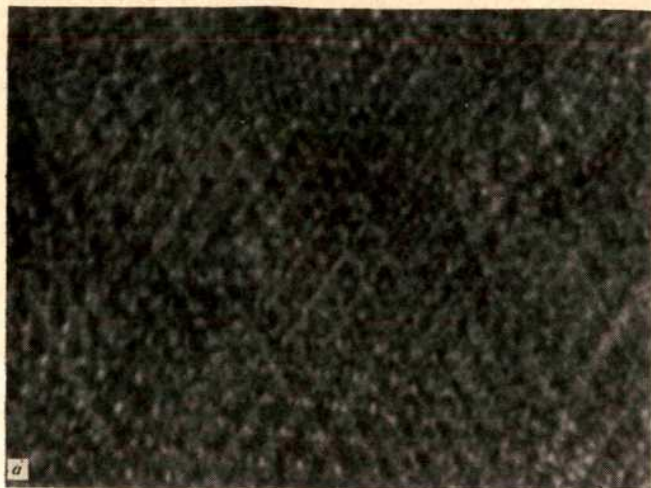


Fig. 3 *a*, A 'first-fit' reconstructed image produced with a stop in the spatial filter plane to eliminate completely the undiffracted beam. *b*, Optical transform of this image. Although the spots are weakened, as compared to Fig. 2*b*, no significant features have been lost.

Attempts are being made to apply the method to the reconstruction of images from electron and X-ray diffraction patterns.

The ability to reconstruct images from a spatial filter and a random image indicates that extreme care must be taken when using spatial filtering methods to improve the quality of very noisy images, or an artefactual structure defined by the spatial filter may be generated in the reconstructed image, no matter whether it was present or not in the original specimen. Clearly, a 'noisy' electron micrograph can act as a random frequency generator, and the use of a spatial filter which is at all an accurate inverse of a suspected structure is to be avoided. Other hazards of spatial filtering have recently been reviewed⁴. The explanation suggested above for the appearance of reconstructed images is a tentative one, and requires further detailed study to prove or disprove it. The basic phenomenon is, however, readily demonstrated.

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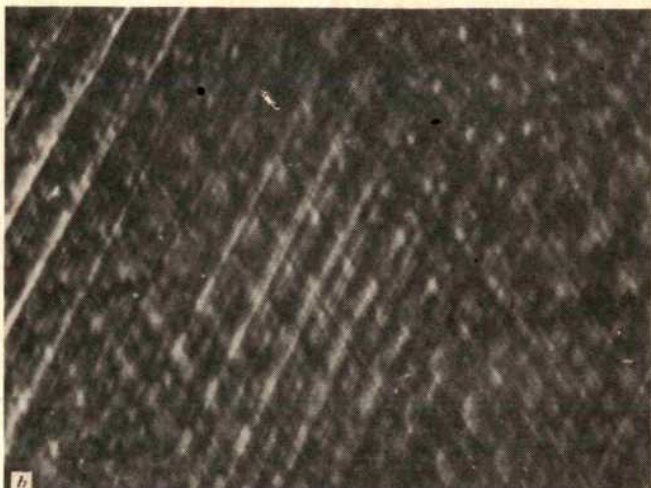
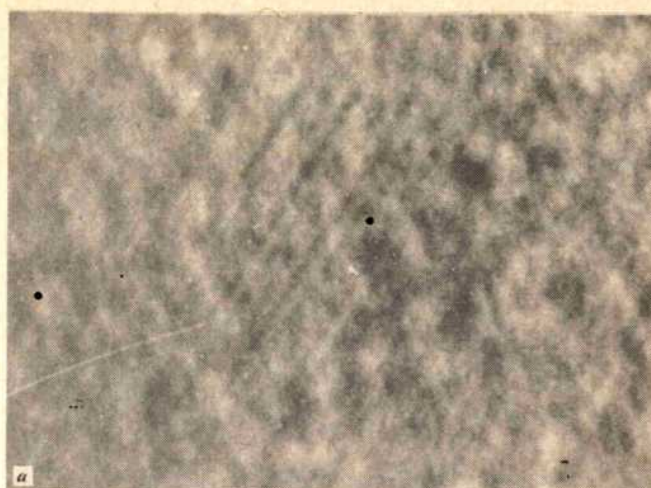


Fig. 4 *a*, A 'first-fit' reconstructed image of rather poor quality, probably due to granularity (visible in the image) in the random frequency generator. *b*, A 'second-fit' reconstructed image, produced by placing the 'first-fit' image in the specimen plane of the diffractometer, with the complementary filter still in position.

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Endocrine Activity retained in Diapause Insect Larvae

DIAPAUSE is a state of arrested development which synchronises insect activity cycles with seasons when food resources are available. Facultative diapause occurs in response to environmental cues such as photoperiod and temperature which influence the endocrine system before the unfavourable conditions arrive^{1,2}. We have now obtained evidence that the currently accepted theory of humoral regulation of larval diapause should be revised. Past research on the pupal diapause of Saturniid moths led to the widely accepted conclusion that larval and pupal diapause result from a failure of the neurosecretory cells of the brain or the corpora cardiaca to release the brain (prothoracotropic) hormone which is required to stimulate the prothoracic glands to secrete the moult-

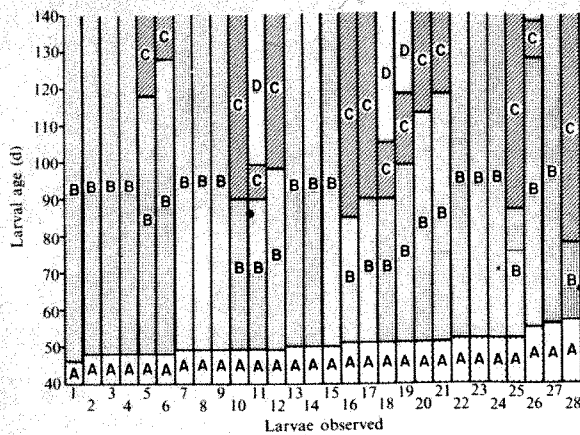


Fig. 1 Bar chart illustrating the occurrence of ecdyses during diapause of twenty-eight mature larvae of *Diatraea grandiosella* held at 23° C; 12 h light, 12 h dark cycle. A, Mature spotted sixth stage larvae; B, immaculate larva; C, immaculate larva which has undergone one ecdysis; D, immaculate larva which has undergone two ecdyses. Under these conditions larvae begin to pupate around 140 d.

ing hormone, ecdysone³⁻⁵. The arrest of growth and moulting and the initiation of diapause have therefore been attributed to the absence of this brain hormone from the haemolymph⁶. Available evidence linking larval diapause with an inactive endocrine system has, however, remained inconclusive⁷⁻¹⁰. Our data indicate that, on the contrary, mature diapause larvae of the southwestern corn borer, *Diatraea grandiosella* Dyar, must retain a functional endocrine system since they undergo stationary ecdyses during diapause. The ability of diapause larvae to undergo stationary ecdyses remains consistent with the concept of diapause as a state of arrested development because the stationary ecdyses do not affect the developmental stage¹¹. (Lüscher used the term stationary ecdysis to describe the ecdysis of the pseudergate larvae of the termite, *Kaloterms flavicollis*, when no progressive development occurs.) We now have evidence to implicate juvenile hormone (JH) in the regulation of this larval diapause.

A Missouri population of *D. grandiosella* which under natural conditions enters diapause in September and pupates in late spring was used for this study. The borers were reared on an artificial diet at 23° C under a 12 h light, 12 h dark photoperiod¹². Under these conditions they passed through six larval stages, reached their mature larval stage around 40 d, and entered diapause. The larvae were then individually transferred to cotton-plugged glass vials containing moist paper strips and maintained under the same regime. Diapause development occurred at a low rate. Pupation began around 140 d, reached 50% around 185 d, and was completed in 210 d. Laboratory-reared and field-collected diapause larvae respond similarly¹³.

A series of randomly-selected larvae was individually observed daily from 40 to 140 d to determine the extent of their moulting activity (Fig. 1). The results show that over a 10 d period between 45 and 55 d each mature larva underwent a stationary ecdysis from a spotted to an immaculate form. This transformation identifies the onset of diapause since the immaculate mature larva which lacks cuticular pigmentation is this borer's distinct diapause form¹⁴. The data also show that after reaching the immaculate stage 50% of the larvae underwent one further stationary ecdysis and 14% two further stationary ecdyses. This phenomenon has been observed in at least 1,500 laboratory-reared and field-collected diapause larvae over the past 2 yr. Each ecdysis which occurred during diapause was typically larval-larval and all larvae retained their immaculate form. Head capsules had a mean width of 2.71 ± 0.05 and 2.56 ± 0.05 mm ($n=10$) before

and after the first immaculate-immaculate ecdysis, respectively. These data yield a ratio of 0.95, which shows that a stationary larval ecdysis had occurred.

According to current thinking, diapause insects are not able to ecdyse. Since our results show that diapause larvae do retain their capacity to undergo stationary ecdyses, even though no growth and differentiation occur, it is important to confirm that the species exhibits a true larval diapause. All the ecological and physiological characteristics of a facultative mature larval diapause are present in diapause larvae of *D. grandiosella*¹⁵. Southwestern corn borers only enter diapause during the mature larval (prepupal) stage, remain inactive, and do not feed. Diapause is induced by simultaneous exposure to low temperatures (<26° C) and short day lengths during the immature larval stages. Although a period of chilling is not required before morphogenesis can be resumed, exposure to warm temperature (>23° C) and long day length accelerates diapause termination¹⁶. Dormancy is therefore genetically programmed and does not occur in direct response to adverse environmental conditions and can only be terminated after a period of reactivation^{1,2}. These traits indicate that this arrested development is a diapause.

The borer has also been shown to exhibit typical physiological adaptations for diapause. In common with other diapause insects, diapause southwestern corn borers have a low respiratory and metabolic rate¹⁶. The oxygen consumption of diapause and mature non-diapause larvae (six replicates of seven larvae each) was measured at 23° C. Newly diapaused larvae were found to have an oxygen consumption of 0.85 ± 0.04 which fell to 0.45 ± 0.01 in mid-diapause, compared with 2.32 ± 0.11 μ l per h/per mg dry weight in non-diapause larvae. The respiratory rate of mid-diapause larvae is therefore about 20% of that of non-diapause larvae¹⁷. Partial dehydration and increased cold hardiness, characteristic of larval diapause^{18,19}, are also found in the southwestern corn borer¹³. Ten days after the spotted-immaculate ecdysis, diapause larvae have a mean water content of only 65% (ref. 14).

Metabolic preparations for diapause, which have already been well documented in other species¹⁶, also occur in the southwestern corn borer. Immature larvae have been found to prepare for diapause by accumulating massive triglyceride reserves in their fat bodies; larvae which have just entered diapause in fact contain about three times as much fat body lipid reserves as non-diapause mature larvae^{20,21}. Metabolic preparation for diapause can also be detected in the gonads; spermatogenesis has been found to occur at a much lower rate in pre-diapause immature larvae than in non-diapause ones²². This evidence therefore proves that *D. grandiosella* exhibits a genetically-programmed larval diapause.

Our findings indicate that the humoral regulatory mechanism of diapause southwestern corn borers differs from the one widely accepted as operating in larval diapause. Histological experiments have shown that larvae of *D. grandiosella* contain an endocrine system composed of median and lateral neurosecretory cells, two corpus cardiacum-allatum complexes, and prothoracic glands comparable with those of other lepidopterous larvae. Since such a high percentage of diapause larvae undergo stationary ecdyses, they must retain an active endocrine system and a high titre of JH because larval-larval ecdyses could not occur without its presence. We have obtained specific information about the humoral relationships of diapause southwestern corn borers. Although detailed results are presented elsewhere²³, the main findings can be summarised as follows: (1) Injecting early and mid-diapause larvae with 20-hydroxyecdysone resulted only in stationary larval ecdyses, showing that a lack of ecdysone does not cause diapause. (2) Neck ligations performed on larvae which had just entered diapause resulted in a premature termination of diapause and pupation of the thoraco-abdominal section, showing that a cephalic factor is necessary for the maintenance of diapause. (3) Injecting 20-

hydroxyecdysone into the thoraco-abdominal section of previously-ligated diapause larvae resulted in a premature termination of diapause and pupation, suggesting that ecdysone only terminates diapause when the cephalic factor is absent. (4) Topical treatment with a JH mimic caused non-diapause mature larvae to become immaculate and enter diapause, suggesting that the JH titre regulates diapause induction. (5) The periodical topical application of a JH mimic to diapause larvae prolonged diapause and increased the number of stationary larval ecdyses, suggesting that the JH titre regulates the maintenance of diapause. We conclude that JH which is produced by the corpora allata in the head is the principal regulatory agent for this larval diapause. Although other investigators have proposed a role for JH in the regulation of larval diapause²⁴, this study has provided the first direct evidence to support its involvement.

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Dislocations in Microtubular Bundles within Spermatozoa of the Coccid Insect *Neosteingelia texana* and Evidence for Slip

THERE is considerable evidence that movement of cilia and flagella depends on slip or sliding between tubules¹⁻³. The evidence, however, is confined largely to cilia and flagella with the common arrangement of a central pair of microtubules surrounded by nine double tubules, the '9+2' arrangement. Coccid insects have filamentous spermatozoa with motility much like flagella and yet they have an arrangement of microtubules quite different from the 9+2 type⁴⁻⁸.

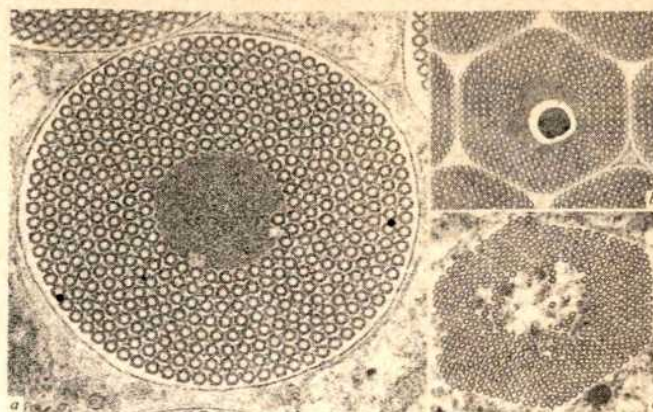


Fig. 1 Cross sections through sperm of *Neosteingelia texana*. a, Microtubules arranged in rings in an unbundled sperm $\times 78,200$. b, Hexagonal microtubular pattern in a sperm tightly packed in a bundle $\times 35,000$. c, Hexagonally arranged microtubules in a disintegrating sperm from a dead insect $\times 35,000$.

Although there is reason to believe that slip between microtubules may be involved in morphogenesis of the corkscrew-shaped region of sperm bundles of the mealybug *Pseudococcus obscurus*⁹, apparently no evidence of slip in movement of coccid sperm has been reported.

The type of slip described in cilia and flagella of the 9+2 type is localised or caterpillar-like¹⁻³. This may be of the same kind as occurs between layers of atoms in a deforming crystal¹⁰. The localised regions at which slip occurs in crystals are known as dislocations. Gliding dislocations, at which slip is occurring locally, have been suggested as an important common denominator of many types of movement at the cellular level¹⁰⁻¹².

Analysis of cross sections of sperm from *Neosteingelia texana* shows that dislocations can be identified in the array of microtubules that make up the bulk of the cell. The pattern of dislocations is not static but depends on the state of the sperm. This observation provides what appears to be the first clear evidence of movement of dislocations at the subcellular level. The movement of the dislocations implies localised slip between microtubules. The type of slip, however, differs from that described in the common form of cilia and flagella: the microtubules slide across one another rather than along one another. This is not to say that there can be no longitudinal slip. It is quite possible that movement involves both kinds.

Fig. 1 shows cross sections of microtubular bundles in three states. Experimental methods and materials are described elsewhere⁸. Developing sperm group into bundles which become motile. While still in the free state a sperm appears round in cross section as shown in Fig. 1a. When the sperm becomes tightly packed into a bundle its outline is roughly hexagonal as in Fig. 1b. Six radial lines at the corners divide this microtubular array into six symmetrically equivalent regions. The microtubules lie on concentric hexagons with rounded corners. A third state occurs when sperm development is interrupted by premature insect death from natural causes. Sperm which normally would be round become hexagonal during their disintegration as shown in Fig. 1c.

Except near the six boundaries in Fig. 1b the microtubules are arranged on a lattice that is rectangular and nearly square. As one approaches a boundary the packing becomes irregular. Crossing the boundary the array becomes rectangular again but with a different orientation. The disintegrating sperm of Fig. 1c shows a similar, if less ordered, arrangement. Boundaries separating lattices of different orientation are known in the literature of crystal physics as grain boundaries. The simplest interpretation of the boundaries in Fig. 1b and c is that they are radial planes

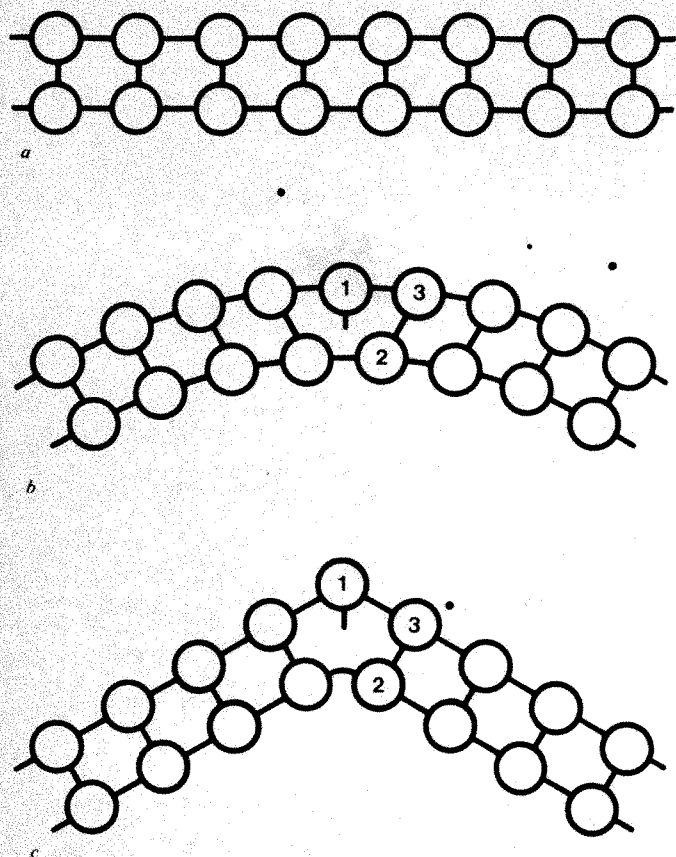


Fig. 2 A perfect and strain-free array of microtubules is shown in (a). Strain in an array of microtubules lying on two concentric circles with a dislocation situated at microtubule 1 is shown in (b). c, Polygonised array with strains each side of the dislocation relaxed. The dislocations in (b) and (c) move as follows: the link from 2 to 3 breaks and forms with 1. The dislocation is then situated at 3, having moved one space to the right.

that separate lattices differing in orientation by a rotation θ about a longitudinal axis. Such boundaries are termed simple tilt boundaries¹³. For perfect hexagons θ would be $\pi/3$ rad. Similar tilt boundaries are found in the arrays of microtubules in heliozoan axonemes¹⁴.

Along the axis of each sperm in Fig. 1 lies a wedge disclination of rotation 2π rad^{10,15}.

A superficial examination of the arrangement of microtubules in Fig. 1a reveals no boundaries. A careful analysis of the pattern of dislocations, however, shows that the boundaries are indeed there and that the pattern of Fig. 1a is simply related to those of Fig. 1b and c.

The neighbouring rings of microtubules in these sperm usually exhibit a difference of six microtubules (Fig. 1a, Table 1). Microtubules arranged at regular intervals in two rows can be matched in pairs if the rows are straight (Fig. 2a) but not if they are curved (Fig. 2b). In the first case the rows may be said to match perfectly all along their length but in the second case the rows match perfectly at the ends only. As one follows the rows away from the ends in Fig. 2b, one finds increasing mismatch or strain until in the middle one finds a region of maximum mismatch. The region of maximum mismatch represents an edge dislocation. The top row has one more microtubule than the other and the extra microtubule may be viewed as being located at the dislocation. The dislocation is a line of maximum mismatch running along the bundle and seen in cross section as a point of maximum mismatch.

Extending the two rows in Fig. 2b repeats the pattern and finally results in a pair of concentric rings. Regions

Table 1 Number of Microtubules in Consecutive Rings from the Most Peripheral (No. 1) to the Most Central Complete Ring in Cross Sections from the Posterior Regions of Forty Sperm

No. of sperm	Microtubules per ring							
	1	2	3	4	5	6	7	8
1	47	41	36	30				
1	47	41	35	30	23			
2	48	42	36	30	24			
1	54	48	42	36	30			
1	54	48	42	36	29			
1	55	49	43	37				
1	57	51	46	39	33			
1	60	52	47	42	36			
1	66	60	54	48	42	36	30	
3	71	65	59	53	47	41	35	
1	72	66	60	55	49	42	37	31
4	72	66	60	54	48	42	36	
5*	73	67	61	55	49	43	37	31
6	73	67	61	55	49	43	37	
1	73	67	61	55	49			
4	74	68	62	56	50	44	38	
3	75	69	63	57	51	45	39	
1	75	69	63	57	51	45		
1	78	72	66	60	54	48	42	
1	79	72	66	60	54	48	42	35

* The sperm cross section of Fig. 1a fits in this group.

of perfect match alternate with regions of maximum mismatch. The number of regions of maximum mismatch and of perfect match is the difference in number of microtubules between the two rings. One therefore expects to find six dislocations equally spaced at angular intervals of $\pi/3$ rad, corresponding to the observed difference of six microtubules.

Freed of all externally applied stresses the two adjacent rows of Fig. 2b are expected to relax into the kinked arrangement of Fig. 2c. The rows now match perfectly everywhere except at the dislocation. Complete rings will become polygons with dislocations located at the corners. In particular if there are six dislocations the polygons will be hexagons. Such a kinked arrangement represents the simplest form of what in crystals is termed polygonisation, in which arrays of dislocations are found at the kinks (ref. 15, page 40).

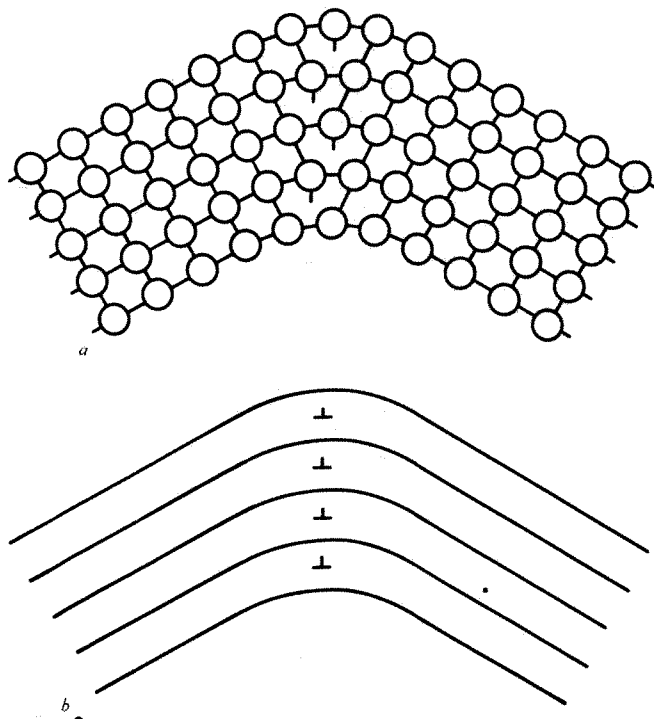


Fig. 3 An idealised view of the arrangement of microtubules (a) and dislocations (b) at corners in Fig. 1b and c. The dislocations lie on radial boundaries.

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Visual Pigment of the Freshwater Stingray, *Paratrygon motoro*

IN general the absorbance spectra of the visual pigments of deep-water and pelagic marine animals are blueshifted compared to those of coastal and estuarine animals, and the pigments of the latter are blueshifted compared with those of freshwater animals. This trend, which correlates with the transmittances of the waters, is best documented for the Osteichthyes (bony fishes)¹. The marine members of this Class, except for some wrasses, have visual pigments based on vitamin A₁ (rhodopsins of $\lambda_{\max}$ 473 to 512 nm). In freshwater Osteichthyes, however, the need for longer-wave sensitivity is met by pigments based on vitamin A₂ (porphyropsins of $\lambda_{\max}$ 523 to 543 nm) or by mixtures of porphyropsin and rhodopsin or, in one case at least (the gwyniad²), by a rhodopsin of high $\lambda_{\max}$ (520 nm).

A similar trend of $\lambda_{\max}$ is apparent in the visual pigments of the Chondrichthyes (cartilaginous fishes). For example, Denton and Shaw³ found that the rhodopsins extracted from three deep-sea sharks ($\lambda_{\max}$ 472 to 484 nm) are in the same range as those of deep-sea Osteichthyes (473 to 490 nm), while the extracted rhodopsins of surface-living sharks and rays have $\lambda_{\max}$ = 497 to 499 nm (ref. 1). Until recently none of the very few cartilaginous fishes that inhabit freshwater has been examined in this respect. Consequently, the report⁴ that the intact retina of the Amazonian stingray, *Paratrygon motoro*, absorbs maximally around 510 nm seems to provide a rare parallel to the visual pigments of the freshwater Osteichthyes, and to raise the question whether its pigment is a porphyropsin or a redshifted rhodopsin.

It should be noted, however, that other bottom-living fishes (Osteichthyes) from the same region were found in that investigation⁴ to have retinal $\lambda_{\max}$ 20 to 30 nm longer than *Paratrygon*. Moreover measurements made on intact retinæ may not be strictly comparable with those made on extracts⁵. Thus one cannot be sure that this apparent difference between the pigments of marine and freshwater rays is real. For this reason we examined a conventional extract.

It was made with three retinæ from two specimens of *Paratrygon motoro* (Mueller and Henle) caught in the Rio Negro near Manaus, over 1,000 miles from the mouth of the Amazon. The retinæ were dissected out, frozen and brought to Sussex for analysis. Facilities for keeping them frozen during transport were not good, and they thawed several times, which probably accounts for the small yield of pigment.

The photoreceptor outer segments were obtained as a minute pellet (by Saito's sugar flotation process⁶) which, after washing with neutral buffer, was extracted overnight with 0.5 ml 3% digitonin solution. The extract was made alkaline with sodium borate and 0.005 M in hydroxylamine. The absorbance spectrum showed only a small amount of pigment, insufficient for homogeneity tests. Consequently it was fully bleached by exposure to white light passed through a Wratten 15 filter. The spectral change in absorbance is shown in Fig. 1. The pigment band agrees with a 499-nm nomogram curve and the product band is characteristic of retinal oxime, confirming that the pigment

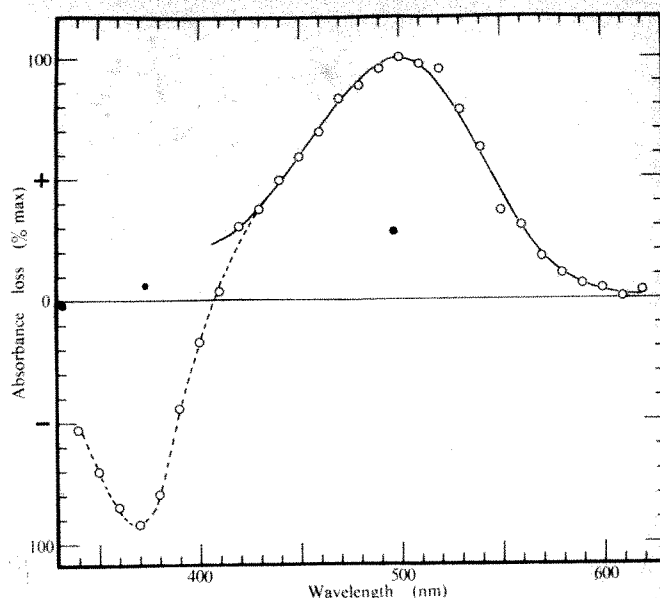


Fig. 1 Normalised difference spectrum (actual $\Delta A_{\max}$ = 0.0115) of the Stingray visual pigment (---) in the presence of 0.005 M hydroxylamine. The product band ($\lambda_{\max}$ ~ 370 nm) is characteristic of the oxime of retinal. —, A 499-nm 'nomogram' pigment. Optical path length 10 mm; volume of extract 0.55 ml, pH 8.45.

is a rhodopsin. Thus there is no significant difference between the rhodopsins of freshwater and marine rays.

Assuming that the 499-nm rhodopsin is the only pigment of the *Paratrygon* retina, it would seem that this animal is not well adapted to its freshwater environment. Its retina, however, is backed by a gold-coloured tapetum⁴ and this will shift the effective sensitivity to longer wavelengths. Although it is possible, therefore, that the presence of a 'normal' rhodopsin means that neither a porphyropsin nor a redshifted rhodopsin could be evolved in this line, it could also mean that a golden tapetum was a simpler solution to the problem. The colour disappears on addition of glycerol⁴, which suggests that, as in other Chondrichthyes, it is an interference phenomenon⁷. The reflectivity might, therefore, have moved to longer wavelengths, during evolution, by a change in the spacing of the tapetal plates.

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Origin of the European Eel

THE controversy about the identity of the European eel was started by Tucker in 1959¹. Contrary to the theory of Schmidt², which assumed that both European and American eels return for spawning to the Sargasso Sea, Tucker argued that it is unlikely that the eels from the European waters manage to return, and that the eels which spawn in the Sargasso Sea are therefore all American. If this were true, the European eel should originate from the same gene pool as the American eel, and have identical gene frequencies, unless differential mortality changes these frequencies.

Morphological and biological evidence, summarised by Deelder³ and more recently by Sinha and Jones⁴, cannot clarify the genetic identity of the European eel. Differences in the frequencies of electrophoretic variants of proteins between American and European eels have been described⁵⁻⁷. For the discovery of conclusive evidence, the variation detected by electrophoresis should be of genetic origin, and differences between American and European eels should be such that they cannot be accounted for by differential mortality of eels possessing particular genotypes. Koehn⁸ has pointed out that "recent literature suggests that allelic isoenzyme variation is responsive to local environmental conditions" suggesting that 'differential intrageneration survival'¹⁴ should be taken into consideration when differences in gene frequency within the geographic range of a species are evaluated. This could apply particularly to a fish like the eel, which during its long larval life is distributed over a wide geographic area and in its second juvenile stage (as an elver) enters a variety of water systems with different conditions. It therefore remains to be shown whether the differences between American and European eels in the frequency of those characters of which the genetic nature has been established within the possible limits^{5,6} are caused either by genetic isolation of the two groups or by environmental influences.

Table 1 Number of Postulated Transferrin Alleles

	Allele				
	A	B	C	D	2N
Iceland	7	34	24	9	74
Scotland	8	17	49	6	80

$$\chi^2 = 14.73_{d.f.} = 3.$$

The genetic control of the transferrin variants detected by Fine *et al.*⁵ is indicated by their phenotypic distribution⁹. Differences in the phenotypic distribution between American and European eels were found⁵, but differences were also observed between eels from different locations in Southern Europe^{10,11}. To explain the latter finding, Drilhon and Fine¹² suggested that the eels in the Eastern Mediterranean reproduce there and form a separate reproductive group. A gene count analysis of the data of Pantelouris *et al.*¹³ on the transferrins of eels from Scotland and Iceland also shows a significant

difference (Table 1). Phenotypic differences in liver esterases of eel from various northern European locations, observed by the same authors, led them to conclude that regional differences in gene frequency may exist for the European eel and to speculate that these differences "may reflect subdivision of populations of the European eel, but they may also be attributed to differential selection"⁷.

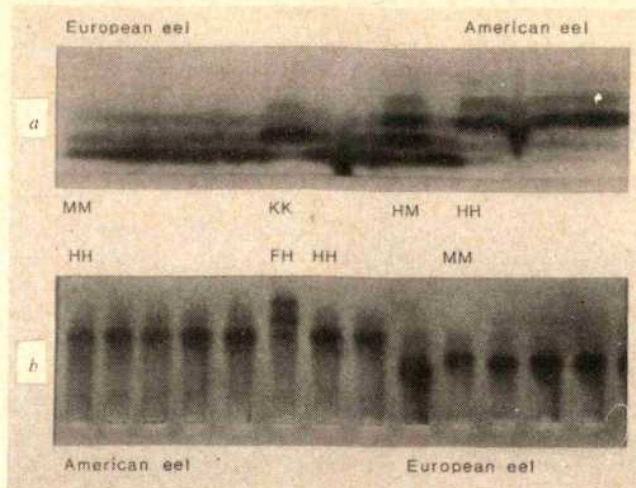


Fig. 1 Livers were homogenised in 1 volume 1% NaCl, buffered at pH 7 and containing 1 mM EDTA, 1 mM MgCl₂ and 1% Triton-X. Homogenates were centrifuged for 15 min at 2,800 r.p.m. and the supernatant was diluted 1:2 or 1:32 for electrophoresis in starch gel or acrylamide respectively. Acrylamide gel slabs were used routinely, but when less well defined patterns were encountered, runs were duplicated in starch gel. *a*, MDH phenotypes in starch gel (11% starch in 0.008 M Tris-citrate, pH 6.7); electrode buffer: 0.223 M Tris-citrate, pH 6.3 (ref. 15); staining fluid: 1,450 mg malic acid, 10 mg NAD, 10 mg 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyl tetrazolium bromide (MTT), 10 mg phenazine methosulphate (PMS) in 100 ml 0.5 M Tris-HCl, pH 8.6 (ref. 16). *b*, MDH phenotypes in acrylamide gel (7% Cyanogum in 0.015 M Tris-citrate, pH 7.0; electrode buffer: 0.15 M Tris-citrate, pH 7.0; staining fluid: 60 mg malic acid, 40 mg NAD, 15 mg MTT, 5 mg PMS in 100 ml 0.05 M Tris-HCl, pH 8.5).

The presence in American eels of a haemoglobin allele, at a frequency of over 3%, that was not found in 748 European eels was considered by Sick⁶ strong evidence against Tucker's one-population concept, unless it is postulated "that in the European part of the population, specimens carrying this allele are exterminated by natural selection".

A recently detected difference in the frequencies of the allozymes of malate dehydrogenase (MDH) between eels from the coast of Maine (USA) and eels from the Azores, Southern Spain, Greece, Holland and Poland now provides conclusive evidence that the eels from the latter five locations are not recruited from the same spawning stock as the eels from Maine. MDH was detected in liver extracts analysed by zone electrophoresis.

Table 2 Observed and Expected Distribution of MDH Phenotypes

Location	FH	HH	HK	HM	HS	KK	KM	KS	MM	MS	MV	N
Poland				3			1		59	7		70
Holland		1		6	2		6		57	3	1	76
Spain			1	8	1	1	3		76	4		94
Greece				4			2	1	53			60
Total (Europe)	1	1.6	1.6	21	3	1	12	1	245	14	1	300
		0.6	0.6	24.2	0.8	0.2	12.4	0.4	240.8	16.1	1.1	
Azores				2					22	1		25
Maine, USA	1	63		6								70

Table 3 Frequencies of Postulated MDH Alleles

Location	MDH ^F	MDH ^H	MDH ^K	MDH ^M	MDH ^S	MDH ^V	N
Poland		0.021	0.007	0.921	0.050		70
Holland		0.066	0.040	0.855	0.033	0.006	76
Spain		0.053	0.032	0.888	0.027		94
Greece		0.033	0.025	0.933	0.008		60
Total (Europe)		0.045	0.023	0.900	0.030	0.002	300
Azores		0.040		0.950	0.010		25
Maine, USA	0.007	0.950		0.043			70

Details of the methods and the major phenotypes observed are given in Fig. 1. The patterns consisted of one or three bands, and agreed with those expected for dimeric molecules of which the peptides are controlled by allelic genes at one polymorphic locus. The patterns were labelled according to the relative mobility of the bands, and genetic control by six alleles (MDH^F to MDH^V) was assumed.

The distribution of the phenotypes observed in the various samples is given in Table 2, together with the expected Hardy-Weinberg distribution for the total of the European samples. In Table 3 the frequencies of the postulated alleles are given. It may be seen from this table that MDH^H has a frequency of 0.950 in the sample of American eel, but ranges in the European samples from 0.021 to 0.066. The sample from the Azores, with a frequency of 0.040, fits well with the European samples. No significant differences were observed between the European samples. The data presented show no differential mortality with regard to the MDH types within the European area, ranging from Greece to Poland. The similarity of the MDH frequencies in the eels from the Azores and from Europe shows that no differentiation of the MDH types takes place during nearly half of the total oceanic migration route of the eel larvae either. Therefore it seems highly unlikely that the difference in MDH frequencies between American and European eels could be due to differential mortality caused by environmental factors. Additional studies of a number of enzyme systems, and studies of esterases and serum proteins, to be published elsewhere, reinforce the conclusion that American and European eels are of different parental origins.

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PCB Residues in Plankton from the Gulf of St Lawrence

ORGANOCHLORINE residues in coastal and oceanic plankton have usually been measured using samples taken at irregular intervals and undifferentiated with respect to particle size^{1,2}, so it has not been possible to relate the variance between samples to temporal differences in supply (or uptake) of contaminants or to differences in plankton composition. Here we describe the variation in polychlorinated biphenyl (PCB) levels with particle size and time in Gulf of St Lawrence plankton.

Nine samples were taken at approximately 10 d intervals from June to August 1972 from a station about 16 km offshore from the northern coast of Prince Edward Island. For each collection a standard No. 20 net (0.5 m diameter, 73 μ m mesh width) was rinsed in isopropyl alcohol and then towed for approximately 20 min through the top metre of the water column near the wake of the boat. Samples were washed with seawater through a stack of Nitex^R screens and split into ten size fractions, with the exception of the collection on June 3 which was split into five parts because it contained few small copepods. The particles retained by each screen were stored in glass vials at -20° C for about 12 weeks before analysis. In addition to these samples, the standing crop of the various size fractions of plankton, including any attendant suspended particulates, on each sampling date, except August 27, was estimated from vertical net tows in the study area.

Organochlorine residues extracted with the acetonitrile based system of Onley³ were cleaned and analysed as described previously⁴. Routine GLC analyses were carried out on a glass column (6 inch $\times$ $\frac{1}{8}$ inch internal diameter) packed with 3% Dexsil 300 (Analabs, Inc.) on 100 to 120 mesh Gas-Chrom Q, operated at 240° C. Comparisons were made with standards of the DDT group and PCBs (as Aroclor 1254^R, Monsanto Ltd). The presence of PCBs was confirmed in selected samples (the August 10 series) by behaviour similar to standards in GLC on a glass column (4 inch $\times$ $\frac{1}{8}$ inch) packed with 10% EGSS-X on 100 to 120 mesh Gas-Chrom Q (preconditioned, Applied Science Laboratories) operated at 195° C and by constancy of peak height ratios and retention times following treatment with ethanolic KOH (ref. 5) or CrO_3 (ref. 6). Although peaks were stable to the latter two treatments, there was some overall loss of recovery attributable to holdup in the interface during extraction. Similar behaviour was observed in PCB-free plankton (August 10, large size fraction) spiked with Aroclor 1254.

PCB concentrations were calculated from average height ratios of several peaks in samples relative to those in standards. Peaks were chosen not to overlap with those of the DDT group. Chromatograms of extracts from the smallest size fractions were remarkably similar to the standards both in retention time and in relative peak height; in larger size fractions, the retention times coincided with standard peaks but the relative peak heights were somewhat different. Treatment with ethanolic KOH or CrO_3 failed

to produce significant changes in the PCB peaks overlapping *p,p'*-DDE or *p,p'*-dichlorobenzophenone, indicating that the DDT group residues were too low to be reliably estimated. Minimum detectable levels of *p,p'*-DDE, *p,p'*-DDT and PCB using these methods were approximately 0.01 to 0.1, 0.02 to 0.2, and 0.2 to 2 p.p.m. wet weight, respectively, depending on sample size.

The possibility that the samples became contaminated during collection can be discounted for two reasons. First, hexane extracts of net material, sampling gear, boat paint (deck and anti-fouling paint), bilge water, and seawater from the wake were free of PCBs. (The anti-fouling paint was particularly suspect, but our analyses were confirmed by the manufacturer who assured us that PCBs were not used during its preparation.) Second, residue levels were statistically independent of the standing crop of plankton in the water column and the amount of material analysed ($P > 0.05$).

and previous estimates can be attributed to differences in mesh size of the collecting net. For example, if we assume that the widely used No. 6 plankton net will fail to catch particles less than the nominal mesh size, 239 μm , but will retain larger particles in the same proportion as a No. 20 net, our results suggest that No. 20 net samples (Table 1, A) will yield, on average, about twice the residues calculated to be present in an equivalent mass of No. 6 net plankton (Table 1, B). Of course these figures are only approximate and will vary according to the composition of the plankton. Nonetheless, our estimates of the probable PCB content of No. 6 net samples are comparable with those found by Risebrough *et al.*²

If the body size/concentration relation found here is applicable to particles smaller than 73 μm , then it seems that even calculations based on No. 20 net samples still underestimate the actual concentration of organochlorines in marine plankton. Cox⁷ seems to have reached a similar

Table 1 PCB Concentrations (p.p.m. Wet Weight) in Gulf of St Lawrence Plankton

Size (μm)	June 3	June 29	July 9	July 17	July 24	August 1	August 10	August 19	August 27
73		7.63	17.06	2.28	7.08	0.68	20.8	3.47	0.41
102		6.53	22.12	0.72	1.30	0.37	3.18	1.53	0.15
153	31	14.43	8.26	0.63	1.01	0.34	8.28	1.95	0.39
202		8.50	7.90	1.45	0.71	ND	0.90	8.55	0.89
253		1.98	1.95	1.34	0.69	ND	0.21	1.74	ND
308	1.7	5.53	3.33	0.67	3.53	ND	0.23	4.73	ND
351		0.29	ND	0.70	1.32	ND	0.27	0.62	ND
505	5.5	0.15	ND	ND	ND	ND	7.57	0.28	ND
760	0.2	0.08	ND	ND	ND	ND	ND	0.18	ND
1,050	3.2	0.10	ND	ND	ND	ND	ND	ND	ND
A	2.84	1.71	3.05	0.66	0.67	0.09	1.17	2.14	0.18
B	1.86	0.21	0.66	0.42	0.40	ND	0.26	1.12	ND
C	93	33	70	5	26	2	33	29	—

A, Mean concentrations found in No. 20 net plankton (includes all size fractions); B, calculated mean concentrations for No. 6 net plankton (based on size fractions $> 202 \mu\text{m}$); C, total PCB residues ($\times 10^{-8} \text{ g m}^{-3}$) associated with No. 20 net plankton. All estimates are weighted according to the standing crop of the different size fractions. ND, Not detectable.

The results summarised in Table 1 show that PCB concentrations were inversely related to particle size, and that this trend persisted in spite of a thirty-four-fold difference in residue levels between composite samples (Table 1, A). This finding is consistent with the known affinity of organochlorines for particulate matter⁷ and indicates that the acquisition of contaminants is directly proportional to particle surface area. Indeed, there is a strong linear correlation ($r=0.95$; $P<0.01$) between the surface to volume ratios of the different size fractions (calculated assuming that plankton are spherical with a radius equal to half the mesh size of the screen) and their average PCB content. This relationship, however, provides only a partial explanation, for on three occasions phytoplankton (principally diatoms) from the 102 μm screens had considerably lower residue levels than the 153 μm fractions (mainly small copepod nauplii).

To our knowledge the 73 μm to 202 μm particles contain the highest PCB concentrations ever reported for natural plankton. Other measurements of coastal and oceanic Atlantic zooplankton range from 0.018 to 0.64 p.p.m. wet weight², whereas samples from the Clyde in Scotland and the Stockholm Archipelago were somewhat lower, ranging from about 0.03 to 0.35 p.p.m. wet weight (recalculated from Jensen *et al.*¹).

Part of this apparent discrepancy between our results

conclusion by noting that most of the DDT residues in seawater are probably bound to particles $< 2 \mu\text{m}$ in diameter which, in turn, account for most of the surface area of suspended particulate material.

Estimates of the total mass of PCBs associated with No. 20 net plankton from the Gulf are given in Table 1, C. Although the overall degree of contamination was very variable, ranging from $93 \times 10^{-8} \text{ g PCB m}^{-3}$ on June 3 to $2 \times 10^{-8} \text{ g PCB m}^{-3}$ on August 1, organochlorines did not seem to accumulate during the study period. On the contrary, the obvious irregularity in residue levels suggests that PCBs entered the plankton in discrete pulses.

For the southern Gulf of St Lawrence, atmospheric input is the most likely source of supply as various organochlorines, including PCBs, have been detected in rainwater and aerial fallout^{8,9}. Moreover, the prevailing wind in summer in this region is from the SSW, meaning that the study area is subject to airborne contaminants originating in the heavily populated St Lawrence River valley and east coast of the United States. This interpretation is supported by Fig. 1, which shows a significant linear correlation ($r=0.86$, $P<0.01$) between PCB contamination (Table 1, A) and the cumulative amount of rainfall 10 to 20 d before sampling¹⁰. Residue levels were not correlated with the amount of rainfall occurring 10 d before sampling, indicating that there is a 2 to 3 week lag between the

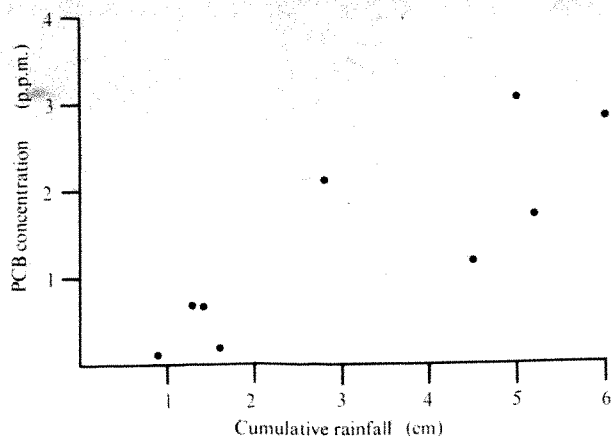


Fig. 1 Relation between the amount of rainfall at Summerside, Prince Edward Island, 10 to 20 d before sampling and average PCB concentrations (p.p.m. wet weight) in No. 20 net plankton.

apparent supply of pollutants and a noticeable uptake by plankton. (The fact that the planktonic community may have been some distance from the station 10 to 20 d before sampling does not affect our argument, as there is an equally good correlation between plankton residues and the average amount of rainfall occurring at Summerside, Prince Edward Island, and a weather station 181 km upstream.)

The evidence presented here indicates that PCBs are transported from the atmosphere to the sea surface, and then on to the plankton. Such a scheme is compatible with current theories^{8,11}, which postulate that organochlorines in surface waters are in equilibrium with those reaching the air-sea interface either adsorbed on particulates or as a vapour, whereas the plankton are assumed to equilibrate with the water-soluble residues. If the atmosphere is indeed the primary source of input to the Gulf, then PCBs will be concentrated near the sea surface after heavy rainfalls. Although the fate of these residues is somewhat uncertain at present, some contaminants are likely to be transported back to the atmosphere by evaporative co-distillation, while the rest would, in time, become dispersed throughout the water column by various biological and physical transport mechanisms.

Cox¹² found that DDT has a half-life of 4 to 10 d in euphausiids. We suggest that PCBs associated with large plankters could be cleared at similar rates, and that this mechanism augmented by a rapid turnover in biomass, especially of small plankters, could account for the low residue concentrations in Gulf plankton following periods of light precipitation. As a general conclusion then, it seems that PCB levels in marine plankton will depend not only on the size composition of the community, but also on spatial and temporal variations in the supply of contaminants.

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Antibody Response to Tapeworm (*Hymenolepis diminuta*) in the Rat

Hymenolepis diminuta, an unarmed, non-invasive tapeworm of the small intestine, is classically regarded as being non-immunogenic in the rat¹. In this host, no pathology is seen², no protective response is stimulated³, and the host-parasite system appears to be maintained in equilibrium. Hopkins *et al.*⁴ suggested that transmucosal antigen transport may occur in such host-parasite systems, and produced evidence⁴ that the rejection of *H. diminuta* in mice is mediated immunologically. Here we present direct evidence of an antibody response to a parasite with no invasive phase, producing no pathology, and living in equilibrium in an environment which may be considered as entirely external to host tissue. This model may find application in the wider field of transmucosal antigen transport and presentation, for example as in food and pollen allergies, as well as serving to illustrate the distinction between the production of an immune response and the development of protective immunity in host-parasite systems.

Eighty-five female Sprague-Dawley SPF rats (200–250 g) were infected by stomach tube under light ether anaesthesia with five or twenty-five cysticercoids of *H. diminuta* dissected from the flour beetle *Tribolium confusum*. Groups of four rats taken at weekly intervals, together with uninfected controls, were anaesthetised with carbon dioxide and bled out by cardiac puncture, and the parasites were recovered and counted. Individual sera for each group were pooled and stored at -70°C . The complete experiment was repeated, the two sets of sera examined independently and the data combined to minimise effects of individual variation. Parasite-specific antibody was detected by 4 h and 72 h homologous passive cutaneous anaphylaxis (PCA) and by the indirect fluorescent antibody method. Antigen was prepared by homogenising freeze-dried adult tapeworm tissue in borate-buffered saline (pH 8.6), sonicating at 21 kHz for 5 min at 0°C and centrifuging at 4°C for 20 min at 20,000g. The supernatant was decanted, a sample removed for protein estimation by the method of Lowry, and stored at 4°C with the addition of 1/10,000 merthiolate as preservative. The insoluble residue was fixed in an ascending methanol gradient to 90%, washed twice in saline and freeze-dried in suitable aliquots to be used as a particulate antigen for fluorescent studies.

The indirect fluorescent antibody technique was performed as described by Kane *et al.*⁵, taking the highest serum titre which gave definite fluorescence as the end-point. For PCA studies, immunoglobulins from a 1 ml sample of serum were precipitated with 50% ammonium sulphate, washed twice, redissolved in 1 ml phosphate-buffered saline (pH 7.2) and dialysed exhaustively against the same buffer. The partially purified immunoglobulins were injected intradermally in doses of 0.05 ml or 0.1 ml into male Sprague-Dawley rats (200–250 g), subsequently challenged intravenously 4 h or

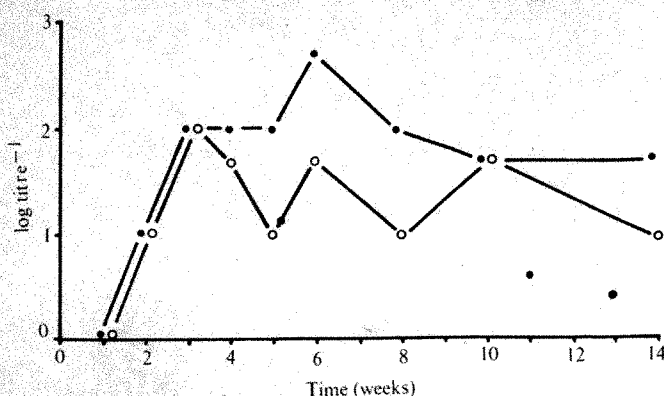


Fig. 1 Evolution of parasite-specific antibody with time, as determined by indirect fluorescence. ●—●, In rats infected with five worms; ○—○, in rats infected with twenty-five worms.

72 h later with 5 mg soluble antigen in 0.5 ml saline together with 1 ml 0.25% Evans blue dye. Reactions were scored 30 min later as previously described⁶.

Table 1 Number of Worms Recovered from Rats Fed Five or Twenty-five Cysticercoids of *H. diminuta*

Age of infection (weeks)	Mean number of worms recovered $\pm$ s.d. 5 Cysticercoids fed	Mean number of worms recovered $\pm$ s.d. 25 Cysticercoids fed
1	4.8 $\pm$ 0.4	24.3 $\pm$ 0.7
2	4.8 $\pm$ 0.4	22.4 $\pm$ 4.0
3	4.5 $\pm$ 0.5	18.8 $\pm$ 4.9
4	4.9 $\pm$ 0.4	16.9 $\pm$ 7.7
5	4.8 $\pm$ 0.7	11.9 $\pm$ 7.1
6	4.3 $\pm$ 0.8	12.1 $\pm$ 7.5
8	4.9 $\pm$ 0.4	12.4 $\pm$ 6.7
10	4.4 $\pm$ 0.8	11.5 $\pm$ 7.5
14	4.8 $\pm$ 0.6	9.5 $\pm$ 11.1

Worm recoveries are summarised in Table 1. Five worm infections were stable, with no evidence of worm loss up to 14 weeks post-infection, confirming the accepted status of *H. diminuta* in the rat. Hosts harbouring twenty-five worm infections, however, showed a progressive loss of worms over the 14 weeks of the experiment. The gradual and incomplete nature of the loss, together with the stability of the low level infection and the similarity of antibody response between the two infection levels, suggests that this loss of worms was not immunologically mediated. The phenomenon may be associated with the 'crowding effect' described by Roberts⁷, and is probably due to simple competition for available resources as the worms increased in size.

The serological data are summarised in Figs 1 and 2. Figure 1 shows the change in parasite-specific fluorescent antibody titre with time for five and twenty-five worm levels.

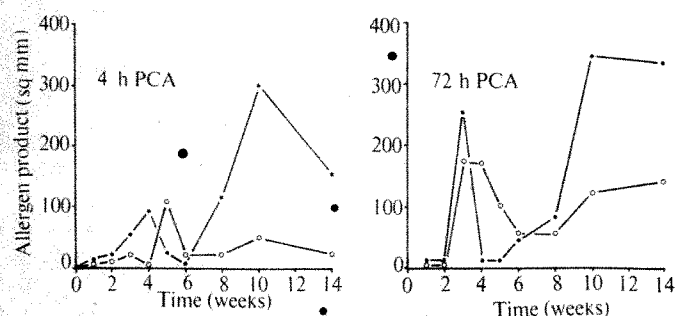


Fig. 2 Evolution with time of parasite-specific antibodies mediating 4 and 72 h PCA. The allergen product was calculated by multiplying the opposing diameters of the reaction at 30 min after challenge together with a subjective 0-4 score for intensity of colour. ●—●, Rats infected with five worms; ○—○, rats infected with twenty-five worms.

Peak titres were reached by week 3, and persisted relatively unchanged through to week 14.

Four hour homologous PCA is thought to be mediated in the rat by a 7S IgG antibody, and 72 h homologous PCA by a true reaginic-type antibody apparently analogous to human IgE⁸. Figure 2 summarises the evolution of 4 and 72 h homologous PCA antibody with time; a biphasic type of response is seen for both antibody types and for both levels of infection. The significance of this feature is not known, although it may possibly reflect qualitative and quantitative changes in immunogens present in the gut as the worms become mature. In this respect, it would be interesting to study in more detail the specificity of early and late antibody populations, particularly in relationship to, for example, the breakdown of gravid proglottids with the consequent appearance of eggs free in the gut lumen of the host.

It is unusual to see both 4 and 72 h PCA antibody responses following helminth infection. Generally such infections lead to production of true reaginic-type antibody but no skin-sensitising 7S IgG, whereas immunisation with parasite antigens leads to production of such 7S IgG⁹. The biphasic type response and the production of both types of skin-sensitising antibody clearly merit further study in relation to less stable host-parasite systems and to non-parasitic allergy.

These data unequivocally demonstrate a broad-spectrum antibody response to an entirely non-invasive, non-pathogenic lumen-dwelling parasite. Antigens must cross intact mucous membranes to be presented in immunogenic form for the development of well known food and pollen allergies; the interaction between the rat and *H. diminuta* may be a valuable model both for study of the mechanisms and pathways whereby such transport may occur, and for the emphasis and examination of the functional distinction between protective and non-protective immune responses.

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Ultrasonic Surveillance of Subatmospheric Decompression

DECOMPRESSION sickness is a recognised hazard of unprotected high altitude flight¹. As attempts to detect circulating bubbles in men during decompression from simulated dives using superficial ultrasonic Doppler devices have apparently been successful^{2,3} we have attempted to detect similar

evidence for bubbles in men undergoing rapid decompression to simulated high altitude.

The one man capsule of a decompression chamber at the Royal Air Force Institute of Aviation Medicine, Farnborough, was used. The ultrasonic equipment was a modified Sonicaid foetal heart detector (operating frequency ~ 2.15 MHz). As for simulated dives³, the transducer was strapped to the chest over the fifth left intercostal space to monitor the ventricles of the heart.

The principle of the ultrasonic Doppler device is well known⁴. Over the heart our instrument gave an audio signal like a heart beat which we recorded.

Abnormal signals associated with hyperbaric decompression have been described as 'plops'². The human ear is still the most sensitive detector for these events. Although the 'plops' appear more clearly when the audio signal has been passed through a 600 to 800 Hz band-pass filter, marginal bubble signals cannot yet be recognised automatically.

Details of the decompressions given in the present series are shown in Table 1. All, except the last, have been used to simulate sudden loss of cabin pressure when training RAF air crew. The most severe pressure ratio is 10.4:1 (run 7). All decompressions were fairly short except the last, which was deliberately extended.

There may well be a critical time as the apparently hazardous procedure known by divers as 'surface decompression'⁷ and by compressed air workers as 'decanting'⁸ is in fact often practised safely⁹.

These procedures are permitted so long as no more than 5 min elapse between leaving pressure and getting to pressure in the recompression chamber^{7,8}. Thus, there may be a 'safe period' of at least 5 min in which significant bubble growth is not expected. As the first eight of our experiments allowed up to 2 min at maximum altitude, giving at most about 6 min above the 18,000 foot threshold, it is possible that no bubbles were detected because insufficient time was allowed. The last run (No. 9) was therefore deliberately extended so that the subject was above the threshold for over 12 min. In spite of exposure to less than 1/5 At for more than 10 min, no bubble signals were heard in the Doppler output either during the decompression or for 5 min thereafter.

We must conclude, therefore, that bubbles will probably be rarely detected in short-term subatmospheric decompressions. This is entirely consistent with the relative incidence of decompression sickness when compared with that found for hyperbaric decompression¹⁰.

We thank the Director General of RAF Medical Services

Table 1 Simulated Decompression of Experienced Personnel Monitored with Superficial Ultrasonic Doppler Devices

Run No.	Subject	Date	Base altitude ($\times 1,000$ feet)	Ascent time (s)	Final altitude ($\times 1,000$ feet)	Period at final altitude including ascent (min)	Symptoms reported	Abnormal Doppler signals
1	PP	February 6, 1973	8	12	40	1	Mild gut pain	None
2	JM	February 6, 1973	8	12	40	2	Mild gut pain	None
3	CW	February 6, 1973	25	3	54	1	None	None
4	AM	February 6, 1973	25	3	54	1	Moderate gut pain	None
5	BP	February 6, 1973	8	30	40	2	Mild gut pain	See text
6	BP	February 6, 1973	8	30	40	1		See text
7	SL	February 6, 1973	8	30	40	2	Toothache	None
8	AM	February 7, 1973	8	12	60	1	Tingling left hand	See text
9	DD	February 7, 1973	8	12	40	10	Sleepy	None

Standard oxygen equipment and, where required, pressure breathing suits were used. Throughout each run ECG and chamber pressure were recorded together, where appropriate, with mask oxygen flow and mask pressure.

All subjects were experienced and able to report any relevant symptoms. The full Doppler signal was recorded throughout each run, which consisted of a 2 min control period at ground level, a gradual ascent to base altitude, a rapid ascent followed by a period at maximum altitude, a gradual descent and a further period of 5 min at atmospheric pressure.

No abnormalities were found in the ECG recordings and no symptoms of decompression sickness were reported with the exception of transient urticaria and petechiae on one run (No. 8). No clear bubble signals were heard. Occasional indistinct abnormal signals were detected in three of the runs (Nos 5, 6 and 8). These did not occur at maximum altitude, but during the recompression. The other runs gave clear heart signals throughout.

The pressure equivalent of a height of 18,000 feet is generally regarded as the safe limit for subatmospheric decompression¹. This corresponded to Haldane's rule² for hyperbaric decompression that the absolute pressure can be halved with safety. In modern diving practice a smaller ratio is used⁶ and we have detected many circulating bubbles with the Doppler apparatus after a simulated decompression of ratio 1.73:1 (ref. 3).

In the present series, no clear evidence for bubbles was found even for subatmospheric pressure ratios of over 10:1. One reason for this may be that the time at altitude was

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Isolation of a New Cardiotoxic Protein from the Edible Mushroom, *Volvariella volvacea*

THE cyclic toxic peptides, phalloidins and amanitins, have been isolated from *Amanita phalloides*; they caused violent emesis and diarrhoea or even death 10 to 24 h after ingestion^{1,2}. Their chemical structures have been elucidated by Wieland³, and the action of the amanitins was found to be the inhibition of RNA polymerase⁴.

We have isolated a new toxic protein from the edible mushroom, *Volvariella volvacea*, which is widely eaten in the Orient and is canned for local consumption and export. From spring to autumn *Volvariella volvacea* forms basidiocarps which appear as ovate bodies with an egg-shaped greyish brown cap that becomes darker at the top. Within 1–2 d, the cap opens, breaking the universal veil, and reaches a diameter of up to 15 cm. The surface of the cap is brown and fibrous, and patterned with darker, radially orientated filamentous streaks. The lamellae are pink, and the stem is surrounded by a dark brown volva. The mushroom has neither smell nor taste.

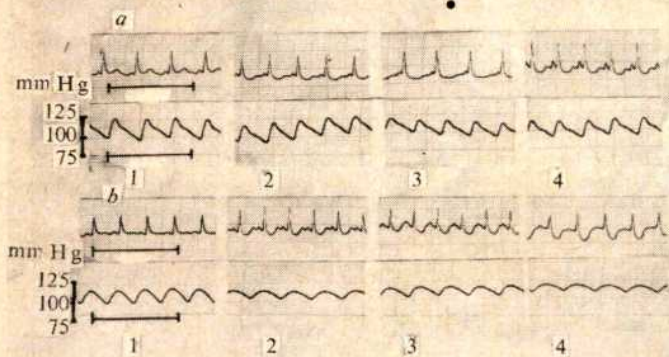


Fig. 1 Effects of volvatxin A on the electrocardiogram and arterial blood pressure of a 2 kg cat, pentobarbital anaesthetised (30 mg per kg body weight intraperitoneally). Upper trace, ECG (lead II); lower tracing, arterial blood pressure. *a*, Injection of 0.7 mg per kg body weight volvatxin A; 1, 0 time; 2, 5 min; 3, 15 min; 4, 75 min. *b*, Injection of 1 mg per kg body weight volvatxin A; 1, 0 time; 2, 3 min; 3, 5 min; 4, 7 min. Bar represents 1 s.

We name the toxic protein obtained from *Volvariella volvacea*, volvatxin. This is extracted from the basidiocarps with cold, 0.8 N acetic acid, 0.016 M mercaptoethanol and 0.001 M EDTA by homogenising in a Waring blender. The proteins that were precipitated between 0 and 50% saturation of ammonium sulphate were collected. After removing the salt by dialysis against 0.016 M mercaptoethanol and 0.001 M EDTA at 4°C for 36 h, the dialysed solution was applied to a DEAE-Sephadex 50A column (5×50 cm) and eluted with 0.1 N acetic acid and 0.016 M mercaptoethanol.

Only one major protein peak was obtained, which was pooled and named volvatxin A. Its toxicity was measured by intraperitoneal injection of various amounts of the toxic protein into male NMRI strain mice, weighing 20±1 g. The LD₅₀ was found to be 1.23 mg kg⁻¹ body weight. Volvatxin A was found to have three major biological activities. The first was a direct haemolytic action: it can completely lyse human group O red blood cells at a concentration of 2 µg ml⁻¹. No phospholipase A activity was detected in volvatxin A. Second, it caused a writhing reaction when administered intraperitoneally. The time of onset was 4 min and a dose of 2–5 mg per kg body weight caused about thirty-six writhing reactions within 10 min of the first writhing reaction. Third, in isolated toad hearts the toxic protein caused ventricular systolic arrest

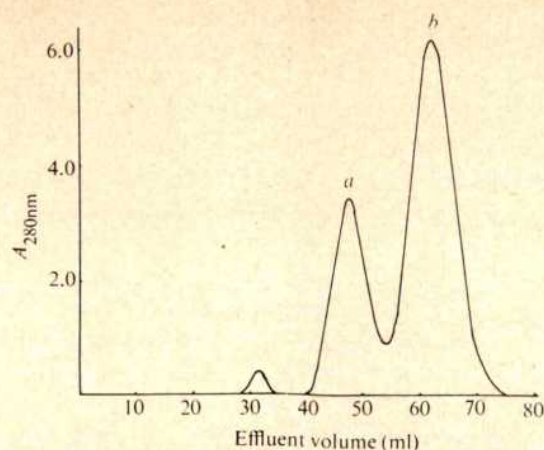


Fig. 2 Chromatogram illustrating the homogeneity of volvatxin A on a column of Sephadex G-75 equilibrated with pH 7.0, 0.01 M phosphate buffered normal saline.

at a dose of 0.1 mg ml⁻¹; in cats an intravenous injection of the protein produced changes in ECG at a dose of 0.7 mg per kg body weight: it depressed the ST segment and inverted the T wave, but no significant changes in blood pressure were noted. The abnormal ECG did not recover until 75 min after the injection (Fig. 1*a*, 2–4). With 1 mg per kg body weight volvatxin A the changes of ECG were much more pronounced and irreversible. A complete atrio-ventricular block with aberrant QRS-T complex and nodal rhythm were observed within 5–7 min after the injection, though the arterial pressure was still normal (Fig. 1*b*, 2–4). The toxicity and biological activities of the toxic protein were completely eliminated by heating at 100°C for 20 min.

The homogeneity of the volvatxin A was tested by gel filtration and the results are shown in Fig. 2. There are

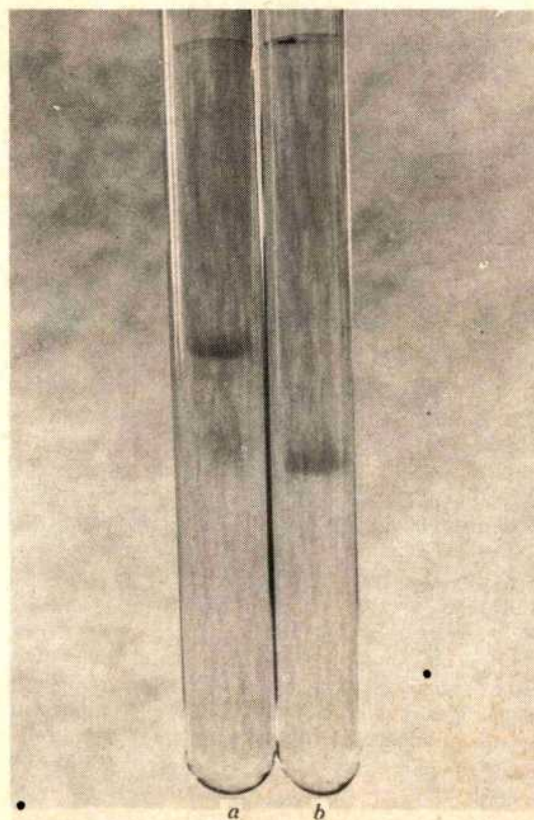


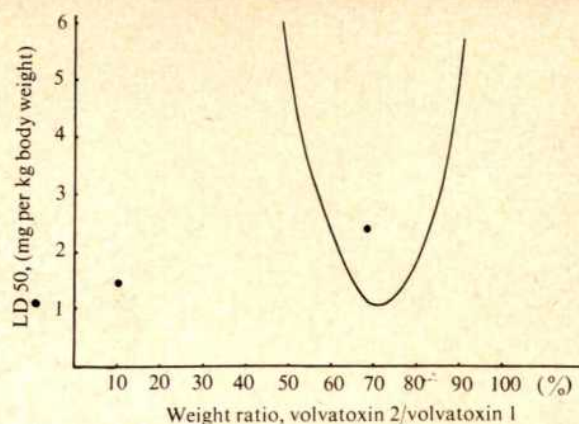
Fig. 3 Sodium dodecyl sulphate gel electrophoresis of volvatxin A1 and A2. The gel on the left shows volvatxin A1 and the gel on the right shows volvatxin A2.

Table 1 Amino Acid Composition Analysis of Volvatoxin A1 and Volvatoxin A2

Amino acid	Volvatoxin 1 residues per 12,500	Volvatoxin 2 residues per 12,500
Lys	9	10
His	1	1
Arg	1	1
Asx	12	11
Thr	10	6
Ser	8	9
Glx	10	11
Pro	3	3
Gly	7	5
Ala	7	8
Cys	—	1
Val	10	6
Met	1	1
Ile	5	5
Leu	9	9
Tyr	5	4
Phe	7	8
Try	5	5
Total	110	104

two major components in volvatoxin A, volvatoxin A1 and volvatoxin A2. The molecular weights of volvatoxin A1 and A2 were found to be 50,000 and 24,000, respectively, by gel filtration⁵ and SDS acrylamide gel electrophoresis⁶. Both proteins are homogeneous with respect to gel filtration and SDS acrylamide gel electrophoresis (Fig. 3). The possibility that volvatoxin A1 is an aggregation product of volvatoxin A2 is excluded by amino acid composition analysis (Table 1) and tryptic map analysis (Fig. 4).

The LD₅₀ of volvatoxin A1 and A2 was determined by intraperitoneal injection and it was found that both proteins lost their original toxicity when they were tested separately and when the LD₅₀ of volvatoxin A1 and A2 was higher than 40 mg per kg body weight. When the two proteins were

**Fig. 5** Toxicity of the mixture of volvatoxin A1 and A2.

mixed together, however, the toxicity of the mixture increased (Fig. 5). The optimal ratio is 1:3 which is the ratio of the two proteins existing in volvatoxin A, and the LD₅₀ of the mixture at the optimal ratio is almost the same as that of volvatoxin A.

The biological activities of the two isolated proteins were investigated. Volvatoxin A2 carries all the haemolytic activity of the volvatoxin A. The minimum concentration for complete lysis is $1.6 \mu\text{g ml}^{-1}$. So far no significant biological activity has been detected in the volvatoxin A1.

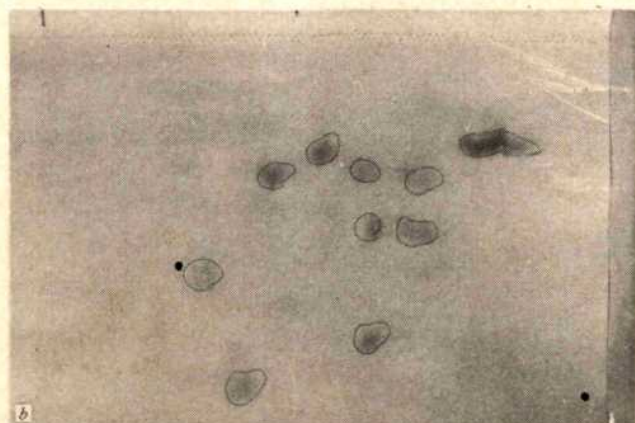
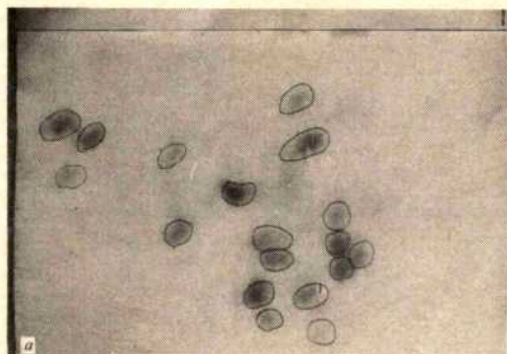
These findings are very similar to those of Hendon and Fraenkel-Conrat⁸, who showed that crotoxin is composed of two kinds of protein, one acidic and one basic. The acidic protein lacks the haemolytic and neurotoxic activity of crotoxin and the basic protein shows only the high, indirect haemolytic activity; a mixture of the two components shows the high neurotoxicity of crotoxin.

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**Fig. 4** Tryptic peptide maps of volvatoxin A1 and A2. Upper map, volvatoxin A1; lower map, volvatoxin A2.

Loss of Bacterial Motility under Pressure

BACTERIAL motility is thought to be ecologically important, especially in environments containing inadequate nutrients. Many bacteria have highly specialised tactic systems that allow them to detect physical or chemical gradients and to swim either to or away from the source. Motility and chemotaxis seem to be important also in bacterial film formation on surfaces and in marine fouling¹.

Microorganisms in the ocean or other bodies of water may be affected significantly by hydrostatic pressure, which increases by about one atmosphere (atm) for every 10 m depth. As

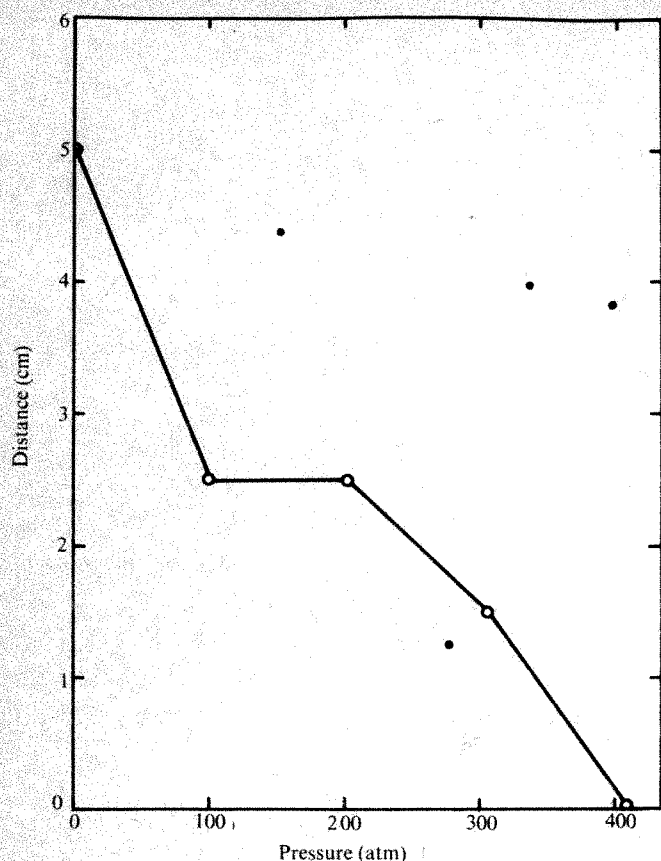


Fig. 1 The effect of pressure on motility of flagellate *E. coli* B275. Capillary tubes were prepared as described in the text, and the position of the moving frontier of bacteria was determined after 75 min at 24° C at the indicated pressures. The medium through which the bacteria moved contained L-serine as energy source but would not support growth of the auxotrophic organism used because it lacked required amino acids. The points shown represent average results of two separate experiments; they indicate corrected values with a 2-cm subtraction for tubes at 1 atm and a 3-cm subtraction for pressurised tubes.

early as 1891, Regnard² reported that pressure inhibits bacterial movement. Subsequent studies³ confirmed and extended Regnard's observations but left the nature of the inhibition undefined. Our recent observations indicate that pressure inhibits both the formation of new flagella and the functioning of previously formed ones.

To assess qualitatively the effects of pressure on motility, we used a soft agar medium and observed growth and movement away from the line of inoculation. Typical results for several bacteria are presented in Table 1. Movement was progressively restricted with increasing pressure, and no bacterium was motile at 306 or 408 atm, even after prolonged incubation, although all of them grew at these pressures.

For more detailed studies we used a streptomycin resistant *Escherichia coli* strain (B275), obtained from Dr J. Adler of the University of Wisconsin, and melting point capillary tubes. A mark was made on each tube 2 cm from one end (end A). The tube was filled from the other end (B) with medium up to the mark. Then end B was plunged into 2% agar gel until the medium moved to within 1 mm of end A. Washed cells were introduced into end A with a finely drawn out Pasteur pipette, and end A was plunged into agar until a 1.5 cm plug was introduced. Finally, the ends of the capillary tubes were sealed with a 1:1 mixture of wax and Vaseline before being placed in test tubes with end A down. The test tubes were filled with sterile water, sealed with serum caps, placed in pressure cylinders, pressurised with a hydraulic pump and laid on their sides. Media used for growth and for motility assays were those described by Adler and Dahl⁴, except that

Table 1 Bacterial Motility under Pressure

Organism	Motility at				
	1 atm	102 atm	204 atm	306 atm	408 atm
<i>Escherichia coli</i>	+++	+++	++	—	—
<i>Serratia marcinorubra</i>	+++	+++	+	—	—
<i>Proteus mirabilis</i>	+++	+++	+	—	—
<i>Salmonella typhosa</i>	+++	++	+	—	—
<i>Bacillus licheniformis</i>	+++	++	—	—	—

Bacteria were inoculated into tubes of soft agar medium by stabbing to a depth of 1.4 cm with marked needles. The medium used for the Gram-negative bacteria was prepared by dissolving 8 g Difco nutrient broth, 25 g Difco peptone and 3 g agar in 1 l of deionised water. The medium for *B. licheniformis* was prepared by dissolving 0.2 g maltose, 0.2 g Difco peptone, 0.4 g Difco yeast extract and 0.3 g agar in 100 ml deionised water. The pH of the solution was adjusted to 7.5, the solution was autoclaved, and then 1.0 ml of 1 M potassium phosphate buffer (pH 7.0) was added. After each tube was inoculated, 1 ml of sterile 2% agar was poured on top to seal the inoculation site. The space above the agar was filled with sterile water, and the tubes were sealed with serum caps before pressurisation. All cultures were incubated at room temperature until growth was clearly apparent in both pressurised and unpressurised tubes—48 h for the Gram-negative bacteria and 72 h for *B. licheniformis*.

vitamin-free casein hydrolysate replaced the amino acid mixture.

For frontier assays, each tube was marked off into eight compartments 1 cm long and broken at the liquid-agar interface at end B. The contents of each compartment were removed with a very fine tip pipette and used to inoculate a tube containing 1 ml of eosin-methylene-blue broth plus 100 µg streptomycin per ml. Tubes were incubated for at least 48 h at 30° C to determine whether or not bacteria had migrated into each compartment.

Figure 1 presents data on the effect of pressure on movement of bacteria in capillary tubes during 75 min of incubation. At 1 atm, the advancing front of bacteria travelled nearly the entire length of the tube; on the other hand, at 408 atm there was no detectable movement. Motility was inhibited at 102 atm, even though growth is unaffected by this low pressure.

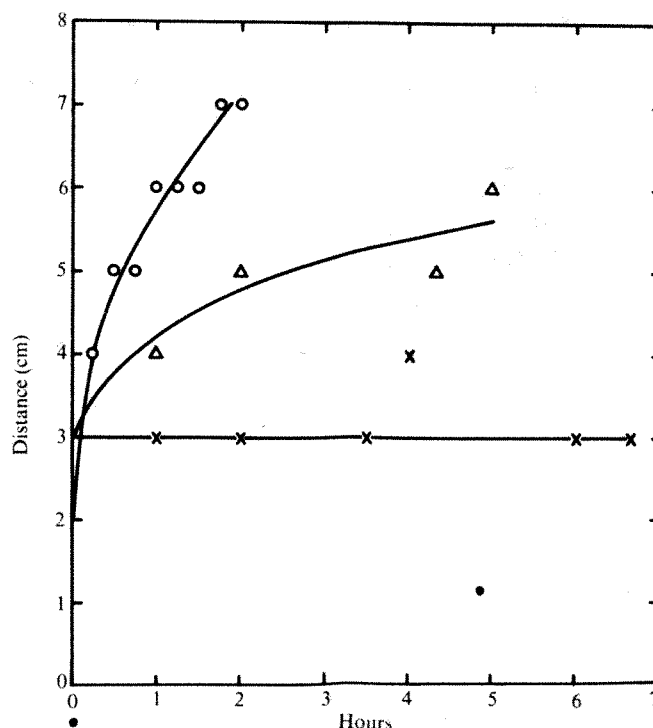


Fig. 2 Time course of movement of *E. coli* B275 along capillary tubes at 24° C and 1 atm (○), 408 atm (△) and 612 atm (×).

Slowing of movement could not be related to increased medium viscosity, which changed less than 1% under pressure⁵.

The points of Fig. 1 were used for a least squares approximation of a linear relationship between distance travelled and pressure. The analysis indicated that the rate of movement decreased by 1.08 cm per 75 min per 100 atm increase in pressure. The apparent activation volume for the inhibitory reaction is equal to $2.30 (d \log k/dP)RT$, where k is the rate, P the pressure, R the gas constant and T the Kelvin temperature. The calculated value of 66.9 ml mol^{-1} is sufficiently large to suggest that inhibition involves some sort of cooperative phenomenon.

Figure 2 presents data from a 7 h experiment. At 1 atm the advancing front of bacteria reached the end of the capillary tube in about 2 h, but at 408 atm the bacteria took about 5 h to travel the distance travelled in 75 min at 1 atm. Movement was stopped completely at 612 atm. The first two compartments of 1-atm tubes always contained bacteria, whereas the first three compartments of pressurised tubes always contained bacteria, even at 612 atm. This difference in zero value is related to pressurisation-depressurisation times and is reflected in the intercepts of Fig. 2.

Although *E. coli* cells were not motile at 612 atm, they retained flagella as indicated by their appearance in smears stained with Leifson's flagellar stain⁶. Gerber and Noguchi⁷ found that *in vitro* aggregation of flagellin to form filaments results in a dilatation of 157 ml per ml of flagellin, and so should be inhibited by pressure. Our results indicate that pressure does not cause disaggregation of flagella *in vivo*.

To see if bacteria can form flagella under pressure, we stained cells grown at various pressures. Inoculum bacteria shown in Fig. 3a were almost devoid of flagella. They were obtained from cultures grown at 37°C in glucose-minimal medium. Glucose acts as a repressor of flagella synthesis⁸, but repression can be relieved by adding cyclic AMP to the cultures⁹. The inoculum bacteria were washed and added to casein hydrolysate medium plus FC-80 (3M Co., St Paul, Minnesota) for growth at 1, 102, 204, 306 and 408 atm. FC-80

is a water-immiscible fluorocarbon which acts as a reservoir for dissolved oxygen to supply cultures in enclosed vessels. As Fig. 3b shows, cells grown at 1 atm synthesised many flagella, those grown at 102 atm synthesised few flagella (Fig. 3c) and those grown at 204, 306 or 408 atm (Fig. 3d, e and f) were nonflagellate. Clearly, flagella synthesis is much more sensitive to pressure than is growth or protein synthesis. Landau^{10,11} found that 272 atm stimulated labelled amino-acid incorporation by this bacterium, 408 atm had no effect, and higher pressures were inhibitory. He also found¹² that enzyme induction was very pressure sensitive and that 265 atm nearly completely inhibited induction of the *lac* operon.

Flagella formation is a complex process involving assembly as well as synthesis of proteins. Perhaps assembly is more sensitive to pressure than is synthesis. Also, it seemed possible that pressure might block induction of synthesis, but we were unable to reverse the inhibitory effect of pressure by adding 5 mM cyclic AMP to cultures.

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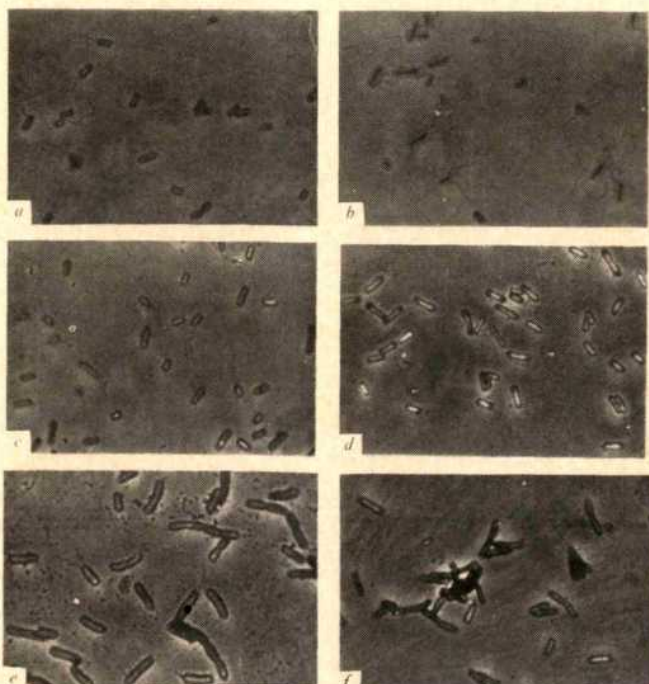


Fig. 3 Effect of hydrostatic pressure on flagellation of *E. coli* B275. Inoculum cells (a) were grown in glucose-minimal medium at 37°C and were subcultured into casein hydrolysate medium for growth at 1 (b), 102 (c), 204 (d), 306 (e) and 408 (f) atm.

Production of Calcite (Calcium Carbonate) Crystals by Soil Bacteria is a General Phenomenon

CERTAIN bacteria form crystals from the solutes in their aqueous environment, and some authors have associated this activity with the extensive deposits of CaCO_3 in such places as the Grand Bahama, in spite of the belief that physico-chemical effects, such as rapid changes in pH, salinity and temperature, are responsible¹⁻⁴. Drew⁵ isolated a denitrifying bacterium able to form CaCO_3 crystals in liquid media and named it "*Bacterium calcis*" (later named *Pseudomonas calcis*⁶). Greenfield⁷ obtained aragonite (another form of CaCO_3) crystals in cultures of *Pseudomonas* in an artificial seawater medium containing Na_2CO_3 or $(\text{NH}_4)_2\text{CO}_3$. Buck and Greenfield reported the same result with marine yeast, and claimed that calcium crystals resulted from the accumulation of calcium deposits on the surface of the cells⁸. McCallum and Guhathakurta⁹ observed calcium carbonate deposition by marine bacteria isolated from Bahama Island sediments, and when these were cultured in different media aragonite crystals formed. Shinano¹⁰ described many marine bacteria able to form crystals in liquid media. Ramos-Cormenzana¹¹ has also reported crystal formation by soil

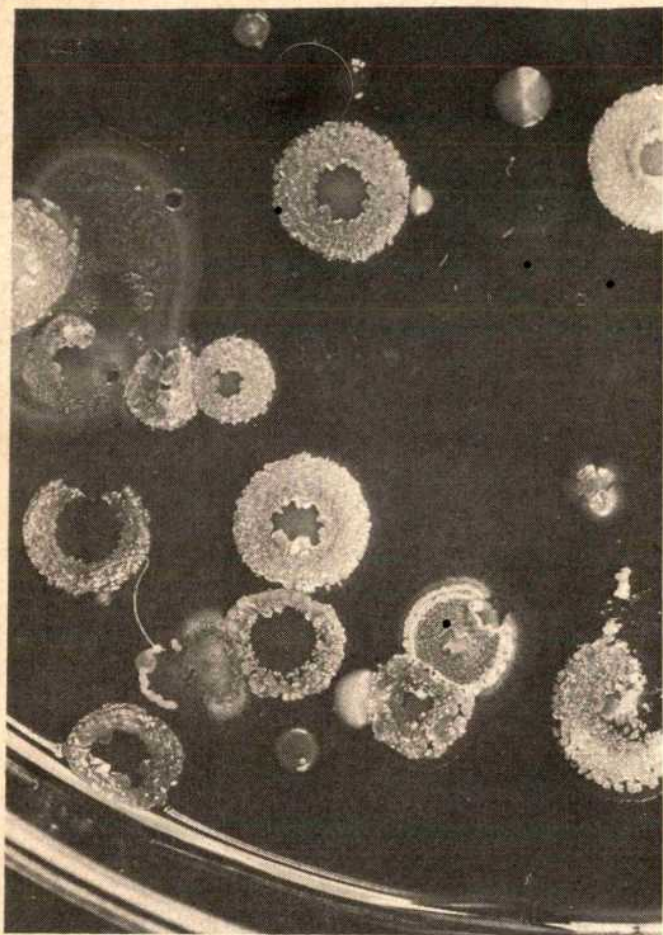


Fig. 1 Macroscopic observations of crystal formation in bacteria. Mixed colonies on plates of B-4 medium after 18 d incubation; colonies which appear free of crystals reveal copious crystalline deposits when examined microscopically.

bacteria in solid media. This, together with the knowledge that previous research concerned only marine bacteria in liquid media, stimulated us to investigate crystal formation by soil bacteria cultured on solid media.

We obtained the best results with B-4 medium, which contains 0.25 g calcium acetate, 0.4 g yeast extract, 1.5 g agar, 1.0 g glucose and 100 ml distilled water, with pH adjusted to 8.0 using NaOH. The same medium without glucose gave good growth and crystal formation, but added glucose speeded the processes. In each case we used uninoculated plates as controls. The appearance of crystals as the bacteria grew could be assessed macroscopically and microscopically. Figure 1 shows several colonies of crystal-forming organisms growing on B-4 medium after 18 d of incubation, and Fig. 2 shows the accumulation of crystals within the colony. The crystals could be scraped off the bacterial growth and washed with water to remove all traces of cells and adhering medium; since they were insoluble in water, they could be washed repeatedly and freed from chemical contaminants.

The crystals were identified physico-chemically by their solubility in HCl, by the Meingen reaction, by infrared spectroscopy, and by petrographic microscopy. The results showed that the crystals were calcite, and X-ray diffraction and comparison with known calcite crystals provided confirmation.

We have isolated 210 organisms able to form crystals on plates of B-4 medium, and found that all the bacteria we isolated from soil, which could grow on B-4, could form crystals. All organisms we have tested from our laboratory collection also formed crystals. These include *Salmonella*

spp., *Azotobacter* spp., *Bacillus pumilus*, *B. subtilis*, *B. megaterium*, *B. cereus*, *B. bulgaricus*, *B. globigii*, *Pseudomonas aeruginosa*, *P. fluorescens*, *Serratia* spp. (non-pigmenting strain), *Citrobacter* spp., *Enterobacter aerogenes*, *E. faecalis* and *Staphylococcus aureus*. They all formed crystals on B-4 agar in 1 to 20 d of incubation. From this we infer that crystal formation is a common phenomenon and that its occurrence is simply a function of the composition of the medium used.

We describe this finding in view of recent reports^{4,10} that only certain bacteria can form carbonate crystals in their growth medium. Shinano¹⁰ isolated 653 cultures of crystal-forming bacteria out of some 5,000 isolates examined. He indicated that no aerobic, Gram-positive, rod-shaped bacteria formed crystals, but we have shown extensive crystal formation by *B. pumilus*, *B. subtilis*, *B. megaterium*, *B. cereus*, *B. bulgaricus* and *B. globigii*.

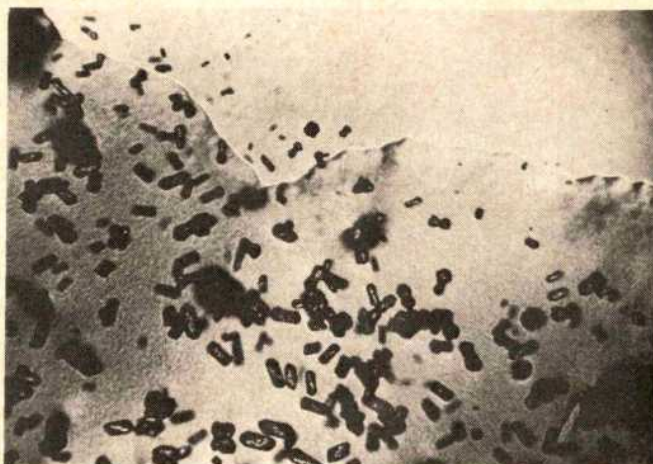


Fig. 2 Microscopic observation of crystal formation by *Proteus vulgaris* (5-d-old culture) in B-4 medium ($\times 27$). The lower part of the photograph shows the cell colony and included crystals, and the top area shows crystals in the medium.

In view of these findings we feel that crystal formation is a function of the medium used and that under suitable conditions most bacteria can form calcite crystals.

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Origin of Chromosome Number Variation in Cultured Plant Cells

CULTURED cells of both animal and plant tissues are characterised by instability of chromosome number and structure^{1,2}. Although there is evidence³ that polyploid plant cell lines may arise from endoreduplicated nuclei in the original explant, the range of chromosome number and structure observed in established cultures strongly points to the origin of these changes during culture. Since the precise distribution of chromosomes at mitotic anaphase is the essential prerequisite for chromosome number stability⁴, this seems the most likely point at which instability could be induced in culture. It has been shown^{6,7} that, in culture, animal cells of various species are characterised by the presence of multipolar mitoses, a feature which would produce daughter nuclei with aneuploid chromosome numbers. Such multipolar mitoses have been briefly noted for plant tissue cultures^{8,9} but their frequencies have not been quantified.

In the present study, the frequencies of bridges, lagging chromosomes and multipolar separations at anaphase and telophase were measured in two suspension culture lines and in seedling root-tip meristems of *Daucus carota* ($2n=18$). The culture lines, originally derived from seedling root segments, and the germinated seedlings, were all of a nucleus stock of *D. carota* donated by Elsoms Ltd (Spalding, Lincs.). Culture line *a* had been grown for thirty-five passages and line *b* for seven passages, each of 18 d duration. Both lines contained 90–95% diploid cells and the remainder tetraploid. The diploid cells of line *a* differed from the normal karyotype by a translocation reducing the chromosome number to 17. Both cultures were maintained on liquid Murashige and Skoog's medium containing 0.1 mg l⁻¹ 2,4-dichlorophenoxyacetic acid (2,4-D) (ref. 10). Such cells were compared with cells from the same initial inoculum subcultured twice on this medium lacking 2,4-D, a treatment which induces embryogenesis^{10,11}. For cytological examination, cells were fixed in 50% (v/v) aqueous formic acid 6 d after transfer to fresh medium, when maximum growth rate and mitotic index were achieved. Root tips, obtained by germination of seeds on moist filter paper, were fixed in Carnoy's solution.

Feulgen-orcein squash preparations of the cultures were analysed for the frequencies of bridges, lagging chromosomes and multipolar configurations at anaphase or telophase. Five slides of each line or treatment were coded and randomised and a total of 200 anaphases plus telophases scored on each slide. A total of 1,000 anaphases plus telophases were scored separately from nine root tip meristems.

As the histogram (Fig. 1) shows, the undifferentiated suspensions of both culture lines showed a significantly ($P<0.05$) higher frequency of multipolar separations than the suspensions initiating embryos and these configurations were absent from the root meristems. The frequency of lagging chromosomes shows a similar trend, though in this respect the root meristem and embryogenic cultures do not differ significantly. In culture line *a*, but not in line *b*, the frequency of bridges was significantly higher than in the root meristems and this probably reflects the presence in line *a* of a population of cells normally containing a dicentric chromosome^{1,9}.

It may be concluded that normal cultural conditions tend to promote abnormalities of the mitotic spindle as evidenced

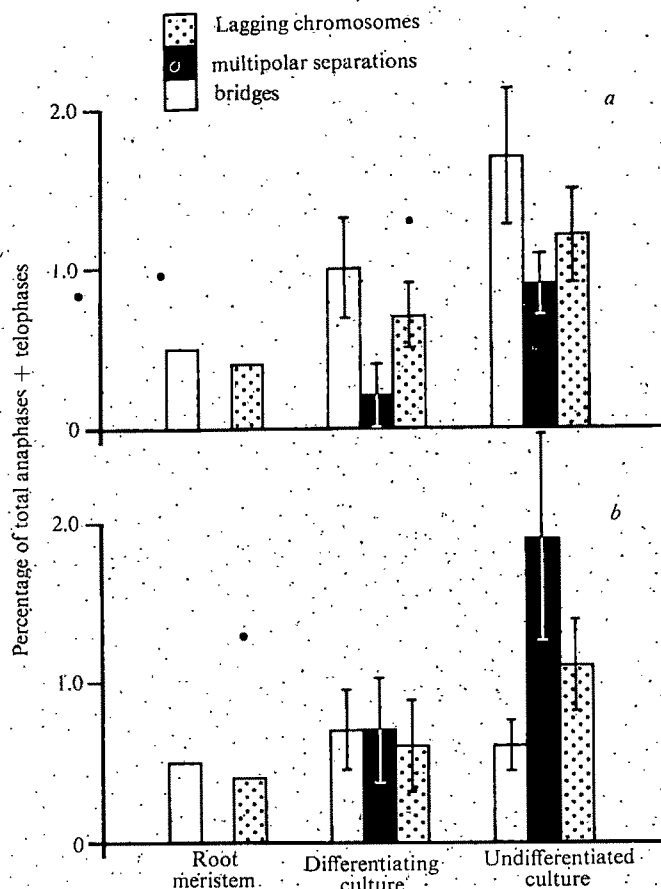


Fig. 1. Frequencies of mitotic abnormalities in two culture lines of *D. carota*; line *a* in its thirty-fifth culture passage, line *b* in its seventh passage.

by the increased frequencies of multipolar separations and lagging chromosomes. It did not prove possible to reliably identify 'C-mitotic' configurations resulting from complete spindle failure, but the partial spindle failure evidenced by multipolar configurations and lagging chromosomes, plus the presence of octoploid and higher chromosome numbers in some carrot cultures, suggests that polyploidisation by spindle failure may occur.

The induction of differentiation in culture seems to reduce the incidence of mitotic abnormalities towards that found in the root tip meristems. In culture, normal mitotic spindle activity could be affected either by the lack of physical organisation of the tissue or by some chemical constituent of the medium. It is, however, not possible here to separate the effects of the increased organisation caused by embryogenesis from the absence of 2,4-D, a substance which at high concentrations is known to induce spindle abnormality^{12,13}. Further, *D. carota* suspensions will not differentiate in the presence of 2,4-D and no diploid line is available which is not embryogenic in the absence of 2,4-D so that suitable controls to distinguish between the effects of 2,4-D and differentiation are not currently possible.

The results demonstrate that mitotic abnormalities likely to give rise to aneuploid chromosome numbers are a significant feature of *D. carota* cultures, and though providing some measure of the rate of production of such aneuploid cells, their final frequency will depend largely on the selective effects of the culture system. The frequencies of mitotic abnormalities can, however, be used to test the various physical and chemical components of the culture which may be responsible for induction of cytological variation, a feature which must be controlled if plant tissue cultures are to be fully exploited in plant breeding programmes.

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RE-ADVERTISEMENT

UNIVERSITY OF OXFORD TUMOUR IMMUNOLOGY

A post is available immediately for research on anti-tumour immunity assayed in vivo. It is supported by an M.R.C. Project Grant for one year. The work will be shared between the Nuclear Physics Laboratory and Dr. I. C. M. MacLennan's laboratory in the Nuffield Department of Medicine. It is of potential practical importance in the radiotherapy and immunotherapy of cancer.

The project needs someone who has a Ph.D. or equivalent experience with mice or cell cultures, and an interest in tumour immunology, radiobiology or cell kinetics is desirable. Candidates must not be over 30, salary up to £2,058 per annum, with F.S.S.U.

Applications, including age, qualifications, the names of 2 referees, and a brief curriculum vitae, should reach Dr. T. R. Munro, Department of Radiation Physics, The Churchill Hospital, Oxford OX3 7LJ, from whom further particulars may be obtained, by January 9, 1974. Telephone Oxford 64841, Ext. 665. (2049)

UNIVERSITY OF MELBOURNE

LECTURESHIP IN THE SCHOOL OF PHYSICS

Applications are invited for this position. Qualifications: Ph.D. with postdoctoral experience.

Duties: Supervision of research students together with undergraduate lecturing or laboratory classes. Experimental physics research is being carried out in high energy physics, diffraction physics and low energy nuclear physics. Further details of research opportunities are available on request to the University. Preference will be given to applicants with interests in experimental high-energy physics. Applicants should have experience in one or more of the following areas: electronic instrumentation, small computers, computing.

Salary: \$A8,698 to \$11,982 per annum.

Consideration will be given to applications for appointment with or without tenure.

Further information is available from the Association of Commonwealth Universities (Appts), 36 Gordon Square, London WC1H 0PF.

Applications close on March 21, 1974. (2027)

UNIVERSITY OF PAPUA
NEW GUINEA
RESEARCH FELLOW
IN AGRICULTURE

Applicants should have a degree in Agriculture or Horticulture with postgraduate experience in intensive vegetable production. A knowledge of breeding techniques is essential and experience in the tropics desirable. The appointee's responsibilities will include investigation into the possibility of intensive vegetable production, especially under conditions prevailing at low altitude, and the breeding of vegetable varieties adaptable to Papua New Guinea conditions. Further information about the Department may be obtained by writing to Professor B. A. C. Enyi.

Salary scales: Senior Lecturer, A\$10,441 to A\$12,089 per annum; Lecturer A\$7,570 to A\$10,205 per annum, plus A\$360 per annum dependants allowance. (These rates include an overseas allowance.) (£1 sterling equals A\$1.57.) Conditions include provision of housing, study leave, annual leave fares, F.S.S.U. superannuation. Applications (2 copies) should include particulars of age, marital status, academic record, qualifications and experience, names and addresses of three referees, a recent small photograph and an indication of estimated starting date.

Further details and conditions of appointment are available from K. R. Long, Secretary, PO Box 4820, University, Papua New Guinea. Closing date: January 31, 1974. (2059)

UNIVERSITY OF OXFORD. LECTURESHIP IN ORGANIC CHEMISTRY. Applications are invited for a University Lectureship in the Dyson Perrins Laboratory, to be held in conjunction with the Fellowship at Wadham College advertised below. Salary in range £1,929 to £4,863 (depending upon age), plus F.S.S.U.—Further particulars from the Administrator, Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, to whom 6 copies of typed applications (only 1 from overseas candidates) should be sent no later than February 4.

WADHAM COLLEGE. OFFICIAL FELLOWSHIP IN ORGANIC CHEMISTRY. The College proposes to elect an Official Fellow in Organic Chemistry from October 1, 1974. Both men and women are eligible. The post is to be held in conjunction with the University Lectureship in the Dyson Perrins Laboratory advertised above.—Applications, giving personal details and a brief statement of academic record, should be sent not later than February 4, 1974, to the Warden, from whom further particulars, including the stipend and teaching duties, may be obtained. (2047)

UNIVERSITY OF PAPUA
NEW GUINEA

LECTURER/SENIOR LECTURER
IN CHEMISTRY

Applicants should have a Ph.D., relevant teaching experience and a background in analytical chemistry or surface chemistry with an interest in soils or mineral or biological materials. The applicant may have had his training in physical, organic or inorganic chemistry. The greater part of teaching duties will be tutoring and demonstrating in elementary chemistry courses based on CHEM study. Scope will be offered for teaching in advanced courses. Information on research facilities and the teaching programme in the Department of Chemistry may be obtained from Professor Drover. It is hoped that the successful applicant will take up duties before May 1974.

Salary scales: Senior Lecturer, A\$10,441 to A\$12,089 per annum; Lecturer, A\$7,570 to A\$10,205 per annum, plus A\$360 per annum dependants allowance. (These rates include an overseas allowance.) (£1 sterling equals A\$1.57.) Conditions include provision of housing, study leave, annual leave fares, F.S.S.U. superannuation. Applications (2 copies) should include particulars of age, marital status, academic record, qualifications and experience, names and address of three referees, a recent small photograph and an indication of estimated starting date.

Further details and conditions of appointment are available from K. R. Long, Secretary, PO Box 4820, University, Papua New Guinea. Closing date: January 31, 1974. (2060)

UNIVERSITY OF ALBERTA

Applications for GRADUATE STUDIES IN PHARMACOLOGY for the degrees of M.Sc. and Ph.D. are invited from students with a background in Biochemistry, Pharmacy, Biology, Chemistry or Medicine. Opportunities exist in Biochemical Pharmacology, Neuropharmacology and Smooth Muscle Pharmacology. Successful applicants may be eligible for financial assistance.

For further information write to: Dr J. S. Charnock, Chairman, Department of Pharmacology, University of Alberta, Edmonton, Alberta, Canada, T6G

CSIRO

DIVISION OF LAND USE RESEARCH

AUSTRALIA

RESEARCH SCIENTISTS

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

GENERAL: The Division of Land Use Research has initiated a research programme on techniques and methodology for non-metropolitan land use planning. A pilot study in association with the NSW State Government and the Centre for Resource and Environmental Studies at the Australian National University is being undertaken on the NSW South Coast. The aim is to integrate both biophysical and socio-economic determinants into a procedure for defining land use options.

FIELD:

REGIONAL
ECONOMIC STUDIES

Ref. 618/367

DUTIES: The Division is seeking a regional economist to undertake a critical evaluative study leading to innovations in, and modifications of, current methods of regional economic analysis as they relate to regional land use planning. Particular topics of interest include (a) the establishment of conservative conditions for the viability of relevant enterprises within a region and (b) the relationship between land use within a region and local income/employment patterns.

QUALIFICATIONS: A Ph.D. degree or equivalent qualifications, together with demonstrable research ability. Experience in a multi-disciplinary research team involving social and biophysical scientists would be an advantage.

FIELD:

TRANSPORT DUTIES

Ref. 618/368

DUTIES: The Division is seeking a research scientist in the field of regional transport studies to investigate the relationship between regional transport networks and regional land use planning. This will include devising methods for the descriptive and normative analysis of transport systems.

QUALIFICATIONS: A Ph.D. degree or equivalent qualifications together with demonstrable research ability. Experience in a multi-disciplinary research team involving social and biophysical scientists would be an advantage.

SALARY: Appointments will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A9,380–\$A14,290 p.a.

TENURE: Either indefinite or fixed term appointments may be negotiated. Indefinite appointments carry Australian Government Superannuation benefits.

APPLICATIONS: Applications stating full personal and professional details, the names of at least two professional referees and quoting the appropriate Reference Number, should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64–78 Kingsway, LONDON WC2B 6BD,

by the 25th January, 1974.

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON D.C. 20036, U.S.A.

(2087)

CSIRO

AUSTRALIA

DIVISION OF ENVIRONMENTAL MECHANICS

• CANBERRA, A.C.T.

RESEARCH SCIENTISTS

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD: FLUID MECHANICS

GENERAL: Research in the Division aims primarily at a basic understanding of the biological and physical processes of the soil-plant-atmosphere system. Energy, water, gas and solute transfers, and their interactions in the system, form a major field of study. Laboratory facilities for soil physics, gas physics, solar radiation, fluid mechanics, micrometeorology and plant physiology are available. Three mobile laboratories are available for field studies. The Division has access to the CSIRO computer network, directly and by teletype link. The staff of the Division includes twelve scientists, supported by technical and administrative staff.

A large, long blower type wind tunnel has been constructed with a flexible roof, flow speeds continually variable from 30 m/sec to a few cm/sec, and 0.1% free stream turbulence. Instrumentation includes an analogue computer and 7 track tape recorder, and hot-wire anemometry. A small digital computer with magnetic tape and disc storage facilities will also be available for direct recording and analysis of data.

DUTIES: To co-ordinate the tunnel research programme, to collaborate with other scientists in the design and conduct of wind tunnel experiments, and to conduct research in fluid mechanics with particular emphasis on tunnel modelling of turbulent transfer processes in the lower atmosphere. This basic project is central to the full exploitation of the tunnel for micrometeorological studies.

QUALIFICATIONS: A Ph.D. degree in physics, engineering or fluid mechanics together with demonstrable research ability and experience in applying these disciplines to problems in the earth sciences. Experience in wind tunnel experimentation is also highly desirable.

SALARY: Appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A9,380–\$A14,290 p.a. An outstanding applicant may be offered appointment at a higher level.

TENURE: This is a three year appointment.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting Reference Number 416/15 should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64–78 Kingsway, LONDON WC2B 6BD
by the 18th January, 1974.

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON D.C. 20036, U.S.A.

(2085)

FERMENTATION SPECIALIST

Fermentation Specialist with experience in large-scale fermentation technology for antibiotic production required, to assume responsibility for technical aspects in major North Italian antibiotics plant. Knowledge of Italian desirable but not essential. Salary according to age and experience.

Write Box 2080, Nature, T. G. Scott & Son Ltd., Clement's Inn, London WC2A 2ED.
(2080)

THE MEDICAL COLLEGE OF ST. BARTHOLOMEW'S HOSPITAL
WEST SMITHFIELD, LONDON EC1A 7BE

Applications are invited for the post of LECTURER IN RADIATION BIOLOGY. Candidates should have a good honours degree in some aspects of radiation Biology. The post involves lecturing at the undergraduate and postgraduate levels to medical and science students. Research facilities are available on different aspects of the interaction of ionizing radiations with biological materials, from cellular to mammalian populations. The main orientation of the research is towards the mechanisms of cancer induction and treatment. The appointment will be on the Non-clinical Lecturers' scale, ranging from £1,929 to £4,548, plus £162 London Allowance, starting salary according to age and experience.

Application forms, which may be obtained from the Secretary, should be returned to the Dean not later than January 31, 1974. (2045)

UNIVERSITY OF EXETER

DEPARTMENT OF BIOLOGICAL SCIENCES

Applications are invited for the post of LECTURER IN BIOLOGICAL SCIENCES tenable from October 1, 1974. Preference will be given to applicants with interests in animal physiology and particularly the physiology of invertebrates, fish or amphibia.

Salary will be on the scale for Lecturers with initial placement within the first four points of that scale £1,929 to £4,548. The appointment will be subject to a probationary period of three years with prospects of permanency thereafter.

Further particulars may be obtained from the Secretary of the University, Northcote House, The Queen's Drive, Exeter EX4 4QJ, to whom applications (8 copies: overseas applicants 1 copy) should be submitted by January 14, 1974. Please quote reference 1/12/3069. (2036)

UNIVERSITY OF NOTTINGHAM

DEPARTMENT OF APPLIED BIOCHEMISTRY AND NUTRITION

Applications are invited for a position of POST-DOCTORAL FELLOW. The successful applicant will be expected to study the synthesis of uric acid in chickens with special reference to its metabolic control and the energetics of its biosynthetic pathway. It is envisaged that extensive use will be made of perfused liver preparations. The salary will depend on qualifications and experience but will be on the lower part of the University Lecturers scale.

Applications, naming two referees, should be made to Professor D. Lewis, Department of Applied Biochemistry and Nutrition, University of Nottingham School of Agriculture, Sutton Bonington, Loughborough LE12 5RD. Telephone Kegworth 2386. Further information can be obtained from Dr. P. J. Buttery at the same address either by telephone or in writing. (2039)

UNIVERSITY OF LEICESTER
MEDICAL SCHOOL

Applications are invited for two posts of LABORATORY TECHNICIAN, one in the Department of Medicine, and one in the Department of Surgery, both posts will be at the Leicester General Hospital initially. These are the first technical appointments to new departments which will expand rapidly over the next few years.

Appointments will be made within the scale £1,848 to £2,163, or £2,007 to £2,382 a year. Initial salary will depend upon age, qualifications and experience. Applications should be forwarded as soon as possible to A. R. Roper, Assistant Registrar, The University, Leicester. (2040)

TECHNICIAN required for PHARMACOLOGY DEPARTMENT, preferably with Part 1 of City and Guilds Course 735 or an O.N.C. in biological sciences. Salary scale £1,440 to £2,292, plus £126 London Weighting. Write, giving age and details of qualifications and experience, to Professor G. W. Bisset, St. Thomas's Hospital Medical School (Uni-

ETON COLLEGE

SENIOR BIOLOGIST OR
BIOCHEMIST

A Biologist with research or teaching experience is required from September 1974 as Head of the Biology Department. The Biology Department is well-staffed and attracts many able pupils: it has modern and well-equipped laboratories and incorporates a famous museum of natural history.

Apply, sending curriculum vitae and the names of two referees, to the Head Master, Eton College, Windsor, Berkshire. (2097)

TEESSIDE POLYTECHNIC

PRINCIPAL LECTURER IN CONTROL
ENGINEERING

Applications are invited from graduates with good honours degrees in engineering or physics and with postgraduate experience in control engineering. The successful candidate will lead a group engaged in teaching Instrumentation and Control Engineering on honours degree and senior technician courses.

Salary: £3,581–£3,989–£4,499.

Application forms and further particulars from Staffing Section, Department N, Teesside Polytechnic, Borough Road, Middlesbrough, Teesside TS1 3BA. Tel: 0642 44176, returnable within 14 days. (2055)

**UNIVERSITY OF
NEWCASTLE UPON TYNE**
MICROBIOLOGICAL CHEMISTRY RESEARCH
LABORATORY

Applications are invited for the position of **SENIOR RESEARCH ASSISTANT** in this unit which is concerned with chemical and biochemical aspects of bacterial cell walls and membranes. Applicants should possess a Ph.D. or equivalent qualification and have some knowledge of the chemistry or biochemistry of carbohydrates or polysaccharides. The work will include a study of the isolation, structure and properties of pneumococcal C-substance. The position, which is supported by the Medical Research Council, is for three years and is in the salary range £1,929 by £129 by £165 to £2,223 per annum, with F.S.S.U.

Applications should be made to Professor J. Baddiley, FRS, Microbiological Chemistry Research Laboratory, The University, Newcastle upon Tyne NE1 7RU. (2034)

**THE MEDICAL COLLEGE OF
ST. BARTHOLOMEW'S HOSPITAL**
WEST SMITHFIELD, LONDON EC1A 7BE

Applications are invited for the post of **LECTURER IN MEDICAL ELECTRONICS** in the Department of Physics. Candidates should have a good honours degree in physics or electrical engineering, with a higher degree in some aspects of medical physics or electronics. The post involves lecturing in post-graduate courses to science and medical students. Research facilities are available on different aspects of the application of physics and electronics to medicine. The appointment will be on the Non-clinical Lecturers' scale, range £1,929 to £4,548, plus £162 London Allowance, starting salary according to age and experience.

Application forms, which should be returned to the Dean not later than January 31, 1974, are obtainable from the Secretary. (2044)

CLINICAL PSYCHOLOGIST

Ph.D. with clinical post-doctoral experience in psychological assessment and treatment of children and/or adults, and research interest in evaluative or clinical areas. Work as part of multidisciplinary team in innovative, progressive community-oriented operation, with teaching and research within McMaster University Department of Psychiatry programmes. Academic rank and salary negotiable.

Applications to: Norman F. White, M.D., Clinical Director, McMaster Psychiatric Unit, St. Joseph's Hospital, Hamilton, Ontario, Canada L8N 1Y4 (2061)

NUTRITIONIST

Provincial Traders Pty. Ltd., Brisbane, Australia, invite applications for the position of Nutritionist to formulate commercial poultry, pig and cattle rations, using the company's analogue as well as digital computers. The successful applicant will also assist with the poultry research programme. Minimum qualifications for this position are a science degree and at least two years' postgraduate experience either in a commercial or academic position related to animal nutrition. Provincial Traders' activities include an integrated broiler operation, stock feed manufacture, oil seed processing, and the production of margarine and related food products. It is a rapidly expanding progressive company with group annual sales in the vicinity of A\$60,000,000.

Applications, stating full personal particulars, qualifications and experience, together with the addresses of two referees, should be forwarded to 'Nutritionist', c/o Personnel Manager, Provincial Traders Pty. Ltd., Box 10 PO, Morningside 4170, Brisbane, Australia. (2068)

MOUNT VERNON HOSPITAL
Northwood, Middlesex HA6 2RN

Department of Cancer Research

Applications are invited for the posts of **RESEARCH ASSISTANT** (graduate) and **LABORATORY TECHNICIAN** to assist in karyotype studies on human tumours and premalignant conditions. Experience of chromosome banding and tissue culture techniques would be an advantage.

Salaries in accordance with qualifications and experience (Universities and Whitley Council scales respectively).

Please reply to Secretary, Department of Cancer Research (tel. Northwood 26111, extension 258). (2049)

Organic Chemist

A young chemist is required in the Biomedical Section of the Development Department to join a small team working on the purification of dyes and reagents. The person appointed is likely to be in the early twenties, and to be a graduate GRIC or perhaps HNC. Salary will be attractive, related to age, experience and qualifications. Modern buildings and facilities within eleven miles of Cambridge. Good fringe benefits. Sports facilities. BUPA Group. Transport to and from Cambridge and Royston. Assistance with resettlement from outside the area.

Contact the Development Manager for details and application form, quoting ref. no: D/202.

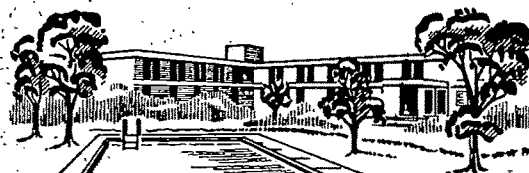


IMAGE ANALYSING COMPUTERS LIMITED

A subsidiary of Metals Research Limited

MELBOURN ROYSTON HERTS SG8 6EJ • TEL ROYSTON (0783) 80611

(2065)

Opportunities Overseas

This appointment is wholly financed by the British Government under Britain's programme of aid to the developing countries.

Kenya

VETERINARY VIROLOGIST

To work within a Virology Research Programme at the East African Veterinary Research Organisation which includes studies of Rinderpest-like diseases with particular reference to Malignant Catarrhal Fever and Nairobi Sheep Disease. Applicants who should normally be citizens of, and permanently resident in, the United Kingdom should have a degree in Veterinary Science with post-graduate experience in Virology. Appointment for 3 years.

SALARY, subject to UK income tax, in range of £3,250-£4,100 p.a. plus a variable tax free overseas allowance in range of £465-£1,130 p.a. Other benefits include free family passages, paid leave, children's education allowances and free accommodation and medical attention. For full details, application form and booklet about Kenya, please apply, giving age and brief details of qualifications and experience, to Appointments Officer.

Foreign and Commonwealth Office,

Overseas Development Administration

Room E301/N, Eland House,
Stag Place, London SW1E 5DH.

(2053)



Caroni Limited Entomologist

A vacancy exists for an Entomologist in Caroni Limited. The Company is the major sugar producer in Trinidad and Tobago and maintains a research station at Carapichaima, Trinidad, where the agricultural problems of sugar cane production are investigated.

The Entomologist will conduct a programme of research into the chemical control, biology and ecology of the Froghopper, a major pest of sugar cane, with the aim of developing integrated control. He will be responsible for advising the Company on control of this pest.

Applicants should have a good B.Sc. Degree in Zoology, Agriculture or related field, and a post-graduate degree specializing in Entomology; training and/or experience in insect ecology would be an advantage. Experience with the control of sugar cane pests would be advantageous but this is not essential.

Salary will depend on the qualification and experience of the appointee. Furnished accommodation will be provided. Pension or gratuity and medical schemes are offered. Suitably qualified persons should apply in writing submitting details of age, training and experience and the names of two referees not later than December 31, 1973, to:

Personnel Manager,
Caroni Limited,
Couva, Trinidad. W.1.

(2069)

Environmental Pollution and Resources Unit

Scientific Research Administrator

up to £4750

This is an important appointment in the Directorate of Research Requirements, London, which functions as "chief scientist" in the Department of the Environment, advising on the formulation, scale and balance of the Department's total research programme.

The successful candidate will be responsible for defining research requirements in the fields of atmospheric and terrestrial pollution, and of water, bulk minerals and other natural resources.

Candidates, aged at least 28, should normally have a 1st or 2nd class honours degree or equivalent in Sciences or Engineering and preferably have had experience of research management. Experience in biological work would be an advantage.

Starting salary within the scale £3647-£4750 according to qualification and experience. Promotion prospects. Non-contributory pension scheme. For full details and an application form (to be returned by 9 January 1974), write to Civil Service Commission, Alencon Link, Basingstoke, Hants, RG21 1JB or telephone BASINGSTOKE 29222 ext 500 or LONDON 01-839 1992 (24 hour answering service). Please quote S/8477.

DIRECTORATE OF RESEARCH REQUIREMENTS

ROTHAMSTED EXPERIMENTAL STATION

HARPENDEN, HERTS. AL5 2JQ

SCIENTIFIC OFFICER to take charge of the Rothamsted Culture Collection of Rhizobium and to assist in related research. Applicants must have a degree, H.N.C. or equivalent in a biological subject, preferably in microbiology. Experience in plant science a recommendation.

Starting salary £1,318 to £1,590, according to qualifications and experience, on scale to £2,177. Superannuation with non-pensionable allowance to offset contributions.

Applications, naming two referees and quoting reference 2142, to the Secretary by January 18. (2074)

UNIVERSITY OF NEW SOUTH WALES SCHOOL OF APPLIED GEOLOGY

LECTURURER

Salary: \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

In the field of engineering geology. High academic qualifications in geology, together with research and/or professional experience in a field of engineering geology, required. Experience in hydrogeology advantageous.

For details of appointment, including superannuation, study leave and housing scheme, write to the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF.

Applications close in Australia and London on February 1, 1974. (2072)

TASMAN VACCINE LABORATORY (U.K.) LIMITED. BIOCHEMIST. Applications are invited from graduates with first or upper second class honours degree in biochemistry. The person appointed will work on ion exchange processes involving macromolecules and new techniques for protein extraction and recovery. Initial salary in range £1,750 to £2,000.—Applications, in writing, and naming two referees, to Dr. R. A. Grant, Tasman Vaccine Laboratory (U.K.) Ltd., Ferndown Industrial Estate, Staplehill, Wimborne, Dorset BH21 7PE. (2048)

DEPARTMENT OF BIOLOGY HARVARD UNIVERSITY

For the forthcoming academic year, this department expects to make at least two appointments at the "ASSISTANT" PROFESSOR level. Fields of interest include plant biology, genetics, immunology and developmental biology. The university is an equal opportunity employer; women and members of minority groups are specifically encouraged to apply.

Please have three professional persons write us concerning you, and send your résumé, together with your most significant publications prior to February 15, 1974, to Chairman, Department of Biology, 16 Divinity Avenue, Cambridge, Massachusetts 02138. (2006)

UNIVERSITY OF HONG KONG

FACULTY OF ENGINEERING AND
ARCHITECTURE

DEPARTMENT OF MECHANICAL
ENGINEERING

LECTURESHIP IN APPLIED MATHEMATICS

Applications from suitably qualified candidates are invited for the above-mentioned post. The successful candidate will be appointed to teach mathematics and its applications to engineering students and to participate in the work of the mechanical engineering department, to which department the Lecturer will be assigned. Candidates should have adequate industrial, research or teaching experience. Annual salary (superannuable) is: HK\$40,800 by HK\$2,760 to HK\$46,320 BAR HK\$49,080 by HK\$2,760 to HK\$68,400. At the time of issue the rate of exchange is £1=HK\$12.00 approximately. Starting salary will depend on qualifications and experience. Salaries for female appointees below HK\$62,880 are slightly lower than given above; equalization of male and female salary scales will be achieved by April 1, 1975.

Further particulars and application forms may be obtained from the Secretary-General, Association of Commonwealth Universities (Appis.), 36 Gordon Square, London WC1H 0PF, or the Secretary to the Council, University of Hong Kong.

Closing date for applications is January 15, 1974.

UNIVERSITY OF BRITISH COLUMBIA

DEPARTMENT OF CHEMISTRY

Graduate Teaching Assistantships

Graduate Teaching Assistantships are available for candidates with high academic records who wish to pursue further studies towards the M.Sc. and Ph.D. degrees in chemistry. Excellent research facilities are available in all areas of modern chemical science, ranging from bio-inorganic chemistry to chemical physics. Beginning stipends range from \$4,350 to \$4,550 per annum and depend on the qualifications and seniority of the graduate student. In addition, many special merit awards are made to those Graduate Teaching Assistants who show excellence in the performance of their duties. Numerous graduate Scholarships are also available for students with outstanding academic records.

Application forms and further particulars may be obtained from the undersigned.

Professor C. A. McDowell,
Department of Chemistry,
University of British Columbia,
Vancouver, British Columbia,
Canada V6T 1W5. (X1930)

(Revised advertisement)

NATIONAL VEGETABLE RESEARCH STATION

PLANT PHYSIOLOGIST

There is a vacancy for a PLANT PHYSIOLOGIST to study the growth physiology of vegetable crops, especially onions, to provide information for a plant breeding programme and for crop culture studies.

Candidates should have a good honours degree in an appropriate biological science and at least two years' relevant research experience. Appointment in the grade of Higher Scientific Officer (£2,076 to £2,667) or Senior Scientific Officer (£2,615 to £3,640), according to experience. F.S.S.U. with 4% per cent allowance to offset contributions. Full particulars and application form (to be returned by January 18, 1974) from the Secretary, National Vegetable Research Station, Wellesbourne, Warwick CV35 9EF. (2024)

UNIVERSITY OF LONDON

CHAIR OF APPLIED MATHEMATICS AT QUEEN MARY COLLEGE

The Senate invite applications for the above Chair, vacant from October 1, 1974. The successful candidate might be appointed Head of Department. Salary not less than £5,625 per annum, plus £162 London Allowance.

Applications (10 copies) should be received not later than February 15, 1974, by the Academic Registrar (N), University of London, Senate House, WC1E 7HU, from whom further particulars may be obtained. (2100)

UNIVERSITY OF LONDON

CHAIR OF BIOCHEMISTRY AT ST. GEORGE'S HOSPITAL MEDICAL SCHOOL

The Senate invites applications for the above Chair. Initial salary to be agreed, but not less than £5,625 a year, plus £162 London Allowance. Applications (11 copies) must be received not later than January 18, 1974 (amended date), by the Academic Registrar, University of London, Senate House, WC1E 7HU, from whom further particulars may be obtained. Candidates who have already applied need not re-apply. (2071)

UNIVERSITY OF READING

RESEARCH ASSISTANT required in Department of Mathematics for three years to work under the direction of Professor J. N. Hunt on theoretical and compositional aspects of sediment transport under tidal conditions with particular reference to the Thames estuary. A good Honours degree in Mathematics or Mathematics and Computing is required and the applicant will be expected to register for a higher degree. Salary £1,002 by £51 to £1,104 per annum, plus higher degree fees.

Apply, quoting Ref. M. 79, to Assistant Bursar (Personnel), University of Reading, Whiteknights, Reading RG6 2AH. (2054)

MARINE SCIENCE TEAM

Geological Oceanographer-Geophysicist, Ph.D., 20 years' experience in continental shelf exploration, research and teaching, with numerous publications and some patents pending, and Biological Oceanographer, M.Sc., specialist in marine microbiology and pollution, presently teaching and operating own research vessel in the eastern Mediterranean, are interested in becoming associated with an aggressive, developing research, academic or industrial organisation, preferably Europe or Mediterranean area. Box 2079, Nature, T. G. Scott & Son Ltd. (2079)

CSIRO

DIVISION OF BUILDING RESEARCH —HIGHETT, VIC.

AUSTRALIA

RESEARCH SCIENTIST

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD:

ARCHITECTURAL ACOUSTICS

GENERAL: The Division of Building Research undertakes research for the benefit of the Australian community especially in relation to its building and construction activities. Particular attention is given to building materials and design; operational and systems research; tropical building; the urban environment and the internal building environment, e.g. in their thermal and acoustical aspects.

Architectural acoustics research is carried on at the Division's site at Highett, Victoria. Large anechoic, reverberation and transmission chambers are available for laboratory studies of acoustical characteristics of building components, and facilities exist for field studies. A comprehensive real-time analysis system is available for rapid processing of acoustical data from either source.

DUTIES: The appointee will be required to take part in the Division's study of acoustical problems in building and in their environs, in particular to initiate research in noise control and/or room acoustics, in the laboratory or in the field. He may be further required to give advice to industry on the application of research results, and to bodies formulating standards of performance in these environmental matters. The appointee may be required to coordinate the work of the existing acoustics group.

QUALIFICATIONS: A Ph.D. degree or equivalent qualifications in physics, engineering or mathematics, together with demonstrable research ability.

SALARY: The appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A9,380—\$A14,290 p.a.

TENURE: The position is available for an indefinite period and Australian Government Superannuation benefits are available.

Applications stating full personal and professional details, the names of at least two professional referees and quoting Reference Number 390/513 should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64-78 Kingsway, LONDON WC2B 6BD
by the 25th January, 1974.

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(2084)

HAILE SELASSIE I UNIVERSITY ETHIOPIA

Applications are invited for the following posts in the Faculty of Science:

- 2 ASSISTANT PROFESSORSHIPS/LECTURESHIPS IN ANALYTICAL CHEMISTRY
- 1 ASSISTANT PROFESSORSHIP/LECTURESHIP IN PHYSICAL CHEMISTRY
- 1 ASSISTANT PROFESSORSHIP/LECTURESHIP IN PHYSICS

Salary scales: Assistant Professor, Eth.\$15,000 to Eth.\$18,750 per annum; Lecturer, Eth.\$13,500 to Eth.\$15,000 per annum. Housing allowance of Eth.\$3,000 per annum, plus dependants' allowance of Eth.\$600 per annum up to five dependants. (81 sterling equals Eth.\$4.85 approximately.) Family passages and baggage allowance.

Detailed applications (2 copies), including a curriculum vitae and naming 3 referees, should be forwarded by airmail, not later than January 21, 1974, to the Dean, Faculty of Science, Haile Sellassie I University, PO Box 1176, Addis Ababa, Ethiopia. Applicants resident in U.K. should also send 1 copy to Inter-University Council, 90/91 Tottenham Court Road, London W1P 0DT. Further particulars may be obtained from either address. (2056)

University of Leeds

RESEARCH FOR SCHOOL SCIENCE MASTERS

Applications are invited from graduate science masters in schools to take part in research in the Procter Department of Food and Leather Science for a period of four weeks in the summer vacation. Two places are available in 1974 and grants to cover expenses incurred are available from the Worshipful Company of Skinners through its Lawrence Atwell's Charity. Examples of topics are the effects of chemical agents on wheat gluten; differentiation of milks by electrophoresis; amino acid-sugar interactions; the chemistry of vegetable tannins; heat conduction in gelatin and agar gels; the preparation of acetates of metals of high valency; the light microscopy of novel food proteins; and the investigation of methods of cleaning old parchments. These topics are selected with subsequent continuation in the school laboratories in mind.

Applications, giving details of career and interests, and the names of two referees, should be sent as soon as possible to Dr H. E. Nursten, The University, Leeds LS2 9JT. (2025)

IMMUNOLOGY

SENIOR TECHNICIAN required to take charge of routine running of expanding laboratories dealing with immunological disorders of the lung. Opportunity for involvement in wide range of research projects. Applicants should hold F.I.M.L.T., F.I.S.T. or equivalent, and have good practical experience of immunological techniques. Salary on M.L.T. Whitley Council Scales. Superannuation N.H.S. transferable.

Apply, giving details of qualifications and experience, to the Secretary, Cardiothoracic Institute, Fulham Road, London SW3 6HP. (2062)

COMMONWEALTH MYCOLOGICAL INSTITUTE

Applications are invited from graduates or those holding appropriate diplomas for a post of **ASSISTANT** in the Culture Collection. Duties include the maintenance of cultures by freeze-drying and other methods, and investigation of new methods and techniques. Starting salary £1,318 to £2,667 (plus Outer London Weighting), according to age, qualifications and experience.

Applications by January 31, 1974, to the Director, Commonwealth Mycological Institute, Ferry Lane, Kew, Richmond, Surrey TW9 3AF, from whom application forms and further particulars may be obtained. (2077)

UNIVERSITY OF LEICESTER

Applications are invited for the post of **LABORATORY TECHNICIAN, GRADE 3**, in the Department of Physiology. Applicants should have a minimum of three years' laboratory experience, preferably in connection with physiology and pharmacology, and possess O.N.C. or O.N.D. and two A-levels with some O-levels, including mathematics and science subjects, or equivalent qualifications. Salary in the range £1,650 to £1,920.

Applications, which must be in writing, stating age, qualifications and experience, giving the names and addresses of two referees, should be sent as soon as possible to the Chief Technician, Department of Physiology, The University, Leicester LE1 7RH. (2081)

CARDIOTHORACIC INSTITUTE

2 Beaumont Street, London W1N 2DX
(Tel. 01-486 3043)

RESEARCH ASSISTANT

Applications are invited from science graduates and suitably qualified personnel for the post of **Research Assistant** in studies of electron microscopy with autoradiography of the heart. Salary not less than £1,560. Opportunities to study for a higher degree.

Application forms available from the House Secretary. (2096)

UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF PATHOLOGY

Applications are invited for the following posts as graduate **RESEARCH ASSISTANTS**:

POST A: To take part in the investigation into the nature of immunological tolerance studied by growing cells in tissue culture systems. Experience in research, and in particular tissue culture techniques, desirable.

POST B: To take part in research involving immunological aspects of cancer research, with particular reference to the functional properties of thymus derived lymphocyte subpopulations. Ph.D. or equivalent degree and experience in immunological research work desirable.

POST C: To become part of a team investigating the human trophoblast and its tumours. Considerable experience with electron microscopy, including special staining techniques and sectioning of monolayer cultures desirable.

Applications in writing (stating Post A, B, or C), giving full details, to the Superintendent, Department of Pathology, Tennis Court Road, Cambridge CB2 1QP. (2099)

NATURE

A vacancy exists for an ASSISTANT EDITOR

for the handling of biological manuscripts, and the supervision of the refereeing process. This job would suit someone with a few years post-doctoral research experience.

Starting salary would be in the vicinity of £3,000.

Apply to the Editor, Nature, 4 Little Essex Street, London, WC2.

Biochemist

for British-American Tobacco Co. Ltd.,
in their Group Research and
Development Centre in Southampton

Applications are invited for the position of **BIOCHEMIST**, graduate level or equivalent, to work on the response of pulmonary tissues to exposure to inhaled materials. A background of work with animal tissues is considered essential, and experience of tissue and cell systems *in vitro* would be an advantage. The person appointed would have an important part to play in the development of experimental biochemistry within a specialised toxicology department.

A highly competitive starting salary will be negotiated, according to qualifications and experience; other conditions of service are first class, and include relocation assistance.

Please write or telephone for an application form to:

N. R. Page, Esq.,
Group Research and Development Centre,
British-American Tobacco Co. Ltd.,
Regent's Park Road,
Southampton SO9 1PE.

Tel. Southampton 777621.

(2046)

TATE & LYLE LIMITED

Group Research and Development

Applications are invited for two posts in an established and developing project involving the production and evaluation of microbial products.

Senior Microbiologist

An experienced Ph.D. is required to conduct research into the biosynthesis of novel commercially important fermentation products. Several years post-doctoral experience is necessary, and a particular interest in biochemistry or cell physiology would be an advantage.

Chemist

A graduate in Chemistry or Biochemistry with an interest in natural products, especially including polysaccharides, sugars or proteins, is required. Experience with methods of structural and analytical chemistry would be an advantage.

Salaries are competitive and will reflect ability and experience. Conditions of employment include a five-day week, free lunches, a non-contributory pension scheme, a minimum of three weeks' holiday and annual bonus.

Applications stating full personal and professional details should be addressed to the Administration Manager, Tate & Lyle Limited, Philip Lyle Memorial Research Laboratory, The University, Whiteknights, P.O. Box 68, Reading RG6 2BX.

(2076)

UNIVERSITY COLLEGE,
GALWAY

LECTURESHIP IN CHEMISTRY

Applications are invited for the above statutory, full-time post. Salary scale £3,450 by £114 (10) to £4,590 per annum, plus family allowances; non-contributory pension scheme. The person appointed will be required to teach and carry out research in inorganic chemistry. The latest date for receipt of applications is January 4, 1974.

Prior to application, further information should be obtained from the Registrar of the College. (1972)

UNIVERSITY OF LONDON
KING'S COLLEGE

DEPARTMENT OF PLANT SCIENCES

There is a vacancy for a POST-DOCTORAL RESEARCH ASSISTANT to study unusual plant amino acids with particular reference to those which are toxic or potentially toxic in man and animals. The appointment, which is supported by the Science Research Council, is tenable for three years, starting salary £1,929 plus £162 London Allowance.

A curriculum vitae and names of two referees should be sent to Professor E. A. Bell, Department of Plant Sciences, King's College, 68 Half Moon Lane, London SE24 9JF, quoting Reference N21/12. (2095)

ROYAL POSTGRADUATE
MEDICAL SCHOOL

GRADUATE TECHNICAL OFFICER required to join the Intestinal Malabsorption group to work on intestinal enzymes of phospholipid metabolism. Salary in range £1,812 to £2,044 per annum.

Applications to the Secretary, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0HS, quoting reference 2/241/N. (2058)

UNIVERSITY OF LEICESTER
SCHOOL OF
BIOLOGICAL SCIENCES

BOTANY DEPARTMENT

Applications are invited for a SENIOR LECTURESHIP OR READERSHIP (within the scale £4,368 to £5,496 per annum) in Plant Taxonomy to take up appointment from October 1, 1974, or as soon thereafter as possible. The person appointed will be responsible for the teaching of taxonomy in the School and for the supervision of the Herbarium (approaching 100,000 specimens), and will be expected to help in the development of the University Botanic Garden.

Applications should reach the Registrar, University of Leicester, by February 23, 1974, from whom further particulars may be obtained. (2035)

UNIVERSITY OF BRISTOL, DEPARTMENT OF Surgery. Applications are invited for the post of RESEARCH ASSOCIATE/ASSISTANT to study the immune responsiveness of patients with breast cancer. Candidates must possess a Ph.D. The post is annually renewable for two years from January 1, 1974, and carries a salary of up to £2,553 per annum. F.S.S.U. according to experience.—Applications in writing, with the names of two referees, to Dr. M. O. Symes, The Medical School, University Walk, Bristol BS8 1TD, as soon as possible, please. (2102)

STRANGEWAYS RESEARCH
LABORATORY

Wort's Causeway, Cambridge CB1 4RN

Applications are invited for the post of RESEARCH ASSISTANT in the Tissue Physiology Department. The work will be concerned with a study of the role of extracellular proteolytic enzymes in invasive human tumour growth. Applicants should have an honours degree in the biological sciences, preferably with an interest in immunology and/or biochemistry. The work will involve the use of immunological, biochemical and immuno-cytochemical methods and cell and organ culture techniques. The successful applicant will be expected to start in January 1974. The salary starts at £1,830 per annum (plus F.S.S.U.) and rises to £2,058 over 3 years.

Applications, outlining previous experience and including the names of two referees, should be sent to Dr. A. R. Poole at the above address. (2043)

CSIRO

DIVISION OF APPLIED CHEMISTRY
FISHERMEN'S BEND, VIC.

AUSTRALIA

RESEARCH SCIENTIST

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD:

POLYMER
CHEMIST-PHYSICIST

GENERAL: The Division undertakes research into a wide spectrum of applied chemical problems and includes a section devoted to research in polymer chemistry.

DUTIES: To carry out research on mechanical properties of mineral and fibre-filled polymeric composites. This will involve the establishment of suitable test procedures and in particular a study of the properties of the polymer-filler interface. To collaborate in other programs of the section involving the physical testing of polymers.

QUALIFICATIONS: A Ph.D. degree in chemistry, physics or physical chemistry or equivalent qualifications, together with demonstrable research ability. Experience in the testing and interpretation of test data for composites is desirable.

SALARY: Appointment will be made within the salary ranges of Research Scientist or Senior Research Scientist: \$A9,380–\$A14,290 p.a.

TENURE: The position is available for an indefinite period and Australian Government Superannuation benefits are available.

Applications stating full personal and professional details, the names of at least two professional referees and quoting Reference Number 586/173 should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64–78 Kingsway, LONDON WC2B 6BD.

by the 25th January, 1974.

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(2088)

MEETING

NATO ADVANCED STUDY INSTITUTE

*Exploitation of
Seismological Networks*

A meeting organised jointly by the Royal Norwegian Council for Scientific and Industrial Research, and Cranfield Institute of Technology, England and sponsored by the NATO Science Committee, will be held from April 22 to May 3rd 1974, in Oslo, Norway.

The meeting will be concerned with the computational and mathematical procedures required for seismic array processing and the function of communication networks used for this purpose.

It is intended to bring together those working in the fields of Computation, Communication, Seismology and related areas—particularly those concerned with the use and implementation of seismic array systems for earthquake and explosion identification.

Lecturers include: Dr. J. Bendat (U.S.A.); Prof. O. Dahlman (Sweden); Dr. E. Husebye (Norway); Dr. B. Kennett (U.K.); Prof. P. Kirstein (U.K.); Dr. R. Lacoss (U.S.A.); Prof. S. Mueller (Switzerland); Dr. D. Simpson (U.S.A.); Dr. H. Thirlaway (U.K.); Dr. D. Weichert (Canada); Dr. P. Willmore (U.K.).

For further information and application for Fellowships to attend, please write to:

Miss M. E. Williamson (Scientific Secretary)
Computing Centre,
Cranfield Institute of Technology,
Cranfield,
Bedford MK43 0AL,
ENGLAND.

(2090)

LECTURES AND COURSES

UNIVERSITY OF DURHAM
M.SC. IN ECOLOGY

The Departments of Botany and Zoology jointly offer a one-year course in Production and Population Ecology, approved by the N.E.R.C. for the award of Advanced Course Studentships.

For further details of the 1974-75 course and application forms write to Dr. Valerie Standen, Zoology Department, Science Laboratories, South Road, Durham. (2038)

MISCELLANEOUS

The Staff of the
STAZIONE ZOOLOGICA DI
NAPOLI

would like to inform the international scientific community that the administration by a Government Commissar will soon terminate. New statutes have been approved and will be implemented in the near future. A permanent annual budgetary support of more than \$1,000,000 has been allocated by the Italian Parliament. The new statutes establish the formation of Administrative and Scientific Councils. Both boards will include members from foreign countries. The scientific and technical staff will be represented in the new Councils and will have the right to propose a candidate for Director. The Director will be elected by the Administrative Council for renewable four-year terms. The Director will carry out research in his own field and co-ordinate the research of the scientific staff and the numerous guest scientists from Italy and many other countries. He is expected to be a good organiser.

The Stazione Zoologica di Napoli carries out research in biochemistry, ecology, embryology and neurobiology of marine organisms. There are well-equipped laboratories, a collecting service, an excellent library, workshops, etc. Enlargement of the permanent staff will be possible, subject to the approval of the Administrative Council. Space and funds are available for the formation of new and for the renovation of existing laboratories. The staff will be pleased to supply further information and welcome suggestions for the development of the institution. Please address correspondence to: Personale (attention G. de Vivo, Secretary), Villa Comunale 80121, Naples. (2063)

FELLOWSHIPS AND
STUDENTSHIPS

UNIVERSITY OF DUNDEE

DEPARTMENT OF MATHEMATICS

RESEARCH FELLOWSHIP

Applications are invited for a Research Fellowship to undertake theoretical studies on the propagation of sound in fluids. Applicants should have appropriate qualifications in mathematics, physics or engineering, but need not have worked in the field of acoustics previously. The appointment will start in 1974 from a date to be mutually agreed and will be for two years in the first instance. Salary range £1,929 to £2,223, with F.S.S.U.

Applications, quoting ref. Est./7773J, and containing the names and addresses of two referees, should be submitted by January 4, 1974, to the Secretary, The University, Dundee DD1 4HN, from whom further particulars may be obtained. (2051)

UNIVERSITY OF BRISTOL
DEPARTMENT OF SURGERY

Applications are invited for a RESEARCH STUDENTSHIP leading to the degree of Ph.D., tenable for three years. The subject of the research would be immunotherapy for malignant disease. The Studentship, which is financed by the R. L. St. J. Harnsworth Memorial Research Fund, provides for a maintenance grant at the appropriate basic rate, plus tuition fees.

Applications, in writing, with the names of two referees, to Dr. M. O. Symes, The Medical School, University Walk, Bristol BS8 1TD, as soon as possible, please. (2103)

UNIVERSITY OF EDINBURGH

School of Artificial Intelligence

TWO RESEARCH FELLOWS are required to work in the Department of Computational Logic, School of Artificial Intelligence. The research of the Department is on automatic theorem-proving and related topics in artificial intelligence.

The applicants' background and experience should be in one or more of the following subjects:

artificial intelligence, computer science, logic and mathematics.

The appointments, funded by a Science Research Council grant, will be for a period from as soon as possible until 30th September, 1975. Renewal thereafter will be dependent upon continued Science Research Council support. The salaries will be on the University lecturer scale in the range £1,929 to £3,378 per annum, depending on qualifications, experience and age. The posts will have normal increments and F.S.S.U. benefits.

Applications, giving curriculum vitae, an account of professional experience and publications, and names of two referees, should be sent as soon as possible to:

Professor B. Meltzer,
Department of Computational Logic,
School of Artificial Intelligence,
8 Hope Park Square,
Meadow Lane, Edinburgh EH8 9NW, Scotland.

Please quote reference 5085.

(2032)

UNIVERSITY
OF WESTERN AUSTRALIA
PERTHFORESTS DEPARTMENT
POSTGRADUATE RESEARCH
FELLOWSHIP IN BOTANY

Applications for the above-mentioned appointment are invited from graduates with a first-class or upper division second-class Honours degree in Botany or those who expect to obtain this qualification before the end of the year, and Forestry or Agriculture graduates whose courses of study have extended over at least four years and who have had appropriate research experience. The Fellowship, financed by the Forests Department of Western Australia, will be tenable for one year initially with prospects of renewal for up to two further years. The value of the Fellowship is \$A3,150 per annum. Any compulsory University fees and an allowance towards fares will be paid. The Fellow shall be required to enrol as a full-time Ph.D. candidate in the Department of Botany and undertake research in a field covering, mycological, physiological or ecological aspects of tree growth in relation to multiple use forestry, or such other fields as may be prescribed. Further information may be obtained from the Head of the Department, Professor J. S. Pate, in the University.

Applications in triplicate stating personal particulars, academic record, research experience, work proposed and details of any special equipment required, should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, by January 12, 1973. Candidates should request two academic referees to write immediately to the Staffing Officer.

Conditions of appointment and application procedure available from the Association of Commonwealth Universities (Apts), 36 Gordon Square, London WC1H 0PF. (2026)

UNIVERSITY OF WESTERN
AUSTRALIA

DEPARTMENT OF MATHEMATICS

POST-DOCTORAL RESEARCH
FELLOWSHIP IN NUMERICAL
ANALYSIS

Applications are invited for a Post-Doctoral Research Fellow to join a project entitled 'Some Boundary Value Problems in Geophysics' that is financed by the Australian Research Grants Committee. The Joint Chief Investigators are Drs. D. G. Hurley and J. Imberger of the Departments of Mathematics and Mechanical Engineering. Theoretical and experimental research is proceeding on problems involving internal gravity waves, seismic waves, and gravitational circulation in cavities, reservoirs and estuaries. The Research Fellow should be an expert in numerical analysis and will be expected to initiate his own research as well as to carry out joint research programmes with the other investigators.

If satisfactory progress is made in the first year the appointment will be a three year one. The salary will be within the range \$A7,270-8,698 p.a. or \$A8,698-11,982 p.a., depending on qualifications and experience. An allowance towards appointment expenses will be available.

Applications in duplicate, stating full personal particulars, qualifications, publications and experience, should reach the Staffing Officer, University of Western Australia, Nedlands, Western Australia, 6009, by February 2, 1974. Candidates should request three referees to write immediately to the Staffing Officer. (2052)



University of Wales Institute of Science and Technology

*Post-Doctoral
Fellowships*

Applications are invited from candidates who hold a PhD and wish to carry out advanced research in any field covered by UWIST.

Fellowships will be tenable for two years from October 1, 1974 and the stipend will be in the range of £1,750 to £2,500.

Further details may be obtained from Registrar's Assistant
UWIST, Cardiff CF1 3NU.

(2098)

We thank A. J. Gibbs and G. A. McIntyre for a copy of their MATCH computer program and to E. Suzuki for discussions.

T. C. ELLEMAN
H. LINDLEY
R. J. ROWLANDS

Division of Protein Chemistry, CSIRO,
Parkville (Melbourne), Victoria 3052

Received August 6, 1973.

¹ Ycas, M. J. *J. molec. Evolution*, **2**, 17 (1972).

² Lindley, H., and Elleman, T. C., *Biochem. J.*, **128**, 859 (1972).

³ Elleman, T. C., *Biochem. J.*, **130**, 833 (1972).

⁴ Swart, L. S., *Nature new Biol.*, **243**, 27 (1973).

⁵ Gibbs, A. J., and McIntyre, G. A., *Eur. J. Biochem.*, **16**, 1 (1970).

⁶ Dayhoff, M. O., *Atlas of Protein Sequence and Structure* (National Biomedical Research Foundation, Silver Springs, Maryland, 1969).

Appearance of *Hipparion* in the Tertiary of the Siwalik Hills of North India, Kashmir and Pakistan

SIMONS *et al.*¹ have discussed the earliest occurrence of *Hipparion*, a tridactyl fossil equid, in the Tertiary of the Siwalik Hills (Pakistan and India). Their statements are confusing and they have misinterpreted one of my publications. Simons *et al.*¹ reject a possible Chinji occurrence of the genus, partly because "Hussain has pointed out that regardless of the validity of occurrence of the *Hipparion* reputed to have been found near the base of the Chinji, the teeth of these specimens are very large. It is implausible that such animals should have preceded in time the small and structurally different species *Hipparion nagriensis* Hussain".

This is a misinterpretation of my work², in which I clearly stated that the presumed Chinji *Hipparion* teeth cannot be morphologically distinguished from those of the Nagri and Dhok Pathan. *H. nagriensis* from the Nagri Formation is no more primitive than the two Dhok Pathan species (*H. theobaldi* and *H. antilopinum*) in dental pattern or size, but it does differ in cheek tooth hypsodonty and especially in certain functionally important features in the structure of the foot. These characters serve to distinguish *H. nagriensis* from *H. theobaldi* of the Dhok Pathan, which Colbert³ had considered to be present from the lower Chinji through the Dhok Pathan Formations. Simons *et al.*¹ have attributed the same stratigraphical range to *H. antilopinum*, which has never been reported except from the Dhok Pathan Formation; they have thus confused this species with *H. theobaldi* and further clouded an already over-complicated issue. In fact, both of these more advanced Siwalik hipparions (*H. theobaldi* and *H. antilopinum*) are on present evidence restricted to the Dhok Pathan Formation. Neither can be said to be more primitive than the other, but they are separated by size differences^{2,3}, and both seem to be derived *in situ* from *H. nagriensis*².

The presence of *Hipparion* in the Chinji Formation is still uncertain. Representatives of the genus may have entered the sub-Himalayan region in latest Chinji or earliest Nagri times. Definite occurrence of *Hipparion* in the Nagri is the most distinctive faunal feature of this time as compared with the preceding Chinji. Similarly, the first local presence of *Hipparion* in the Vallesian of Spain is the most distinctive feature by comparison to the preceding Vindobonian. In the next younger Dhok Pathan Formation, two

hypsodont teeth and more advanced foot structure than the Nagri *Hipparion*². Similarly, several Turolian *Hipparion* species in Europe are more advanced than the typical Vallesian species (*H. catalaunicum*). On this basis, it is possible to suggest tentatively that the base of the Nagri is correlative with the beginning of the European Vallesian and a similar correlation of the Dhok Pathan and the Turolian is here suggested. Such correlations, however, should be confirmed by other evidence such as entire fauna, flora and absolute dates.

S. TASEER HUSSAIN

Department of Anatomy,
College of Medicine,
Howard University,
Washington, DC

Received March 5, 1973.

¹ Simons, E. L., Pilbeam, D., and Boyer, S. J., *Nature*, **229**, 408 (1971).

² Hussain, S. T., *Bayer. Akad., Wiss., Abh.*, NF 147 (1971).

³ Colbert, E. H., *Trans. Am. phil. Soc.*, NS26 (1935).

GENERAL

What Children Do in Spite of Adults' Hypotheses

Bryant and Trabasso¹ suggested that Piaget was wrong when he claimed that children below about 6 yr of age are incapable of making transitive inferences of quantity.

They proposed that the difficulty encountered by the children Piaget tested was not one of transitivity but one of memory, and that therefore it was sufficient to overcome this problem with a modified technique to show up the idea of transitivity in young children.

Bryant and Trabasso's attack focused on this summary of Piaget's view of transitivity: "Piaget and his colleagues propose that the young child cannot infer, for example, that $A > C$ from the information that $A > B$ and $B > C$. . . the child is unable to coordinate the first two, separate items of information in order to reach the correct inferential conclusion about A and C".

If we are interpreting Bryant and Trabasso correctly, they are making an important and legitimate point in emphasising a more basic aspect of transitivity than Piaget, but we feel that their definition is rather different from Piaget's, and that therefore they cannot be justified in claiming that Piaget was "wrong".

Piaget's "definition" of transitivity²⁻⁵ is linked with the whole structure of his system, and in particular with the idea that, for a judgment to be truly an inference, it must be "operational". For this reason, when Piaget studies transitivity using the seriation task for example, the child is only considered to "succeed" if he can "anticipate" the correct actions; if he has a programme or method to proceed, and thus shows no hesitations; or if he is able to perform modifications of the original task (such as insert a new stick into the already assembled sequence) to show that he has understood the ideas involved.

Thus, by concentrating only on the idea that transitivity consists of the ability to combine two asymmetrical relations to deduce a third, Bryant and Trabasso are discarding the Piagetian concept in which, for a behaviour to be a true inference, the child must be able to make use of it in a

be that the mere fact of combining the two pieces of information $A > B$, $B > C$ into a third, $A > C$, constitutes an inference. It follows that any test of this elemental kind of transitive inference must be designed in as direct a way as possible, to avoid factors which in a practical situation might prevent the child displaying his ability. Piaget's insistence on "operationality" makes his experiments indirect and complicated, and so his experiments may lead children to fail even though they possess Bryant and Trabasso's elemental transitivity idea.

But just as it is necessary to minimise factors which might lead a child to fail to make an inference he is in fact capable of making, it is also necessary to minimise the possibility that he accomplishes the task in question using extraneous spatial or perceptual clues not requiring an inference to be made at all. Thus, as Bryant and Trabasso point out, it is insufficient to test for the notion of transitivity using a seriation task in which there are only three rods, as there is a simple labelling strategy which permits a solution without requiring the notion of transitivity: A is bigger than B, therefore A is big, B is bigger than C, therefore B is big and C is small. But B cannot be both big and small, so it is neither. Another example of an alternative strategy not requiring the notion of transitivity is the idea, also put forward by Bryant and Trabasso, that if the children are shown and remember the actual sizes of each individual rod, they will have no trouble deciding on the pairs which they have not seen.

The existence of this fairly obvious alternative strategy means that Bryant and Trabasso's first experiment is not strong evidence that the children were actually making elemental transitive inferences, as in this experiment the children were allowed to see the actual sizes of all the rods. But their second ("no visual feedback") experiment was designed to obviate this problem by never showing the children the actual lengths of the rods. Even so, we feel that this second experiment cannot offer convincing evidence for the existence of their elemental transitivity notion in 4 yr old children because we are able to propose two other types of strategies which could have been adopted and which would succeed equally well without requiring the idea of transitivity. These strategies and the experiments we performed to test whether they are being used (experiments II, III and IV) are described here, but first we describe experiment I, in which we replicate Bryant and Trabasso's second experiment and investigate their claim that memory limitations play an important role in transitivity experiments.

In experiment I, only a slight difference in memory criterion distinguishes our experiment from Bryant and Trabasso's second ("no visual feedback") experiment. The material consisted of five sticks of decreasing lengths, each one of separate colour. The sticks were presented protruding slightly above a screen which hid their actual lengths. Beginning with the first adjacent pair AB, and going on through BC, CD to the last pair DE, or alternatively starting with the last and going to the first, the children were trained to point out the bigger and smaller stick of the pair. Ten children were trained in increasing order, and ten in decreasing order. Each pair was trained individually until a criterion of eight out of ten correct choices had been obtained, and then the experimenter passed on to the next pair.

The second phase of the training period began after all the pairs had been learnt to criterion; the series of four pairs were shown in a random sequence till on each pair the child had responded correctly twice in succession. (This is where the difference with Bryant and Trabasso occurs: their performance criterion was six times in succession.) At no time were the children shown the actual lengths of the sticks.

In the test phase of the experiment, the children were shown all possible pairs of sticks, including those non-adjacent ("transitive") pairs on which they had not been

trained. The ten possible pairs were shown in random order four times each, giving a total of forty responses per subject. The child was not informed if his choice was correct.

The experiment was performed on a group of children of about the same age (4 yr 1 month) as Bryant and Trabasso's youngest age group (4 yr 5 month).

Table 1 Percentages of Correct Choices ($A > B > C > D > E$) for Twenty Children, aged 3 yr 10 month to 4 yr 4 month (Mean Age 4 yr 1 month) in Experiment I

	B	C	D	E
A	73	86 (61)*	93	97
B		84	82 (64)*	97
C			76	92 (70)*
D				92

Four responses on each pair were made by each child.

All scores are significantly above chance, as assuming that the four individual responses of a child on each pair are independent, the score for twenty subjects on any pair differs from chance at the 0.001 level if it exceeds 67.3% (χ^2 test).

* Limit values predicted by Bryant and Trabasso's calculation according to which correct choice on a transitive pair might require independent recall of both underlying pairs: $P_{BD} \leq P_{BC} \times P_{CD}$. Using this hypothesis the actual scores found should be less than the values in parentheses. This is clearly not the case.

The results, shown in Table 1, are compatible with those of Bryant and Trabasso, all scores being better than chance at the 0.001 level. But two aspects of our data cast doubt on Bryant and Trabasso's interpretations.

First, the performance on the unlearned pairs shows that the children perform much better than one would predict if they had to remember and combine the individual adjacent pairs to make a decision.

Table 2 Comparison of Experiment I (Ours) with Bryant and Trabasso's (B + T) Results for Twenty Children (Mean Age 4 yr 5 month)

Correct choices for unlearned pairs (%)						
	AC	AD	AE	BD	BE	CE
Ours	86	93	97	82	97	92
B+T	98	93	97	82	90	88
B+T - Ours	+12	0	0	0	-7	-4
Correct choices for learnt pairs (%)						
	AB	BC	CD	DE		
Ours	73	84	76	92		
B+T	98	89	87	94		
B+T - Ours	+25	+5	+11	+2		

Four responses per pair per child.

Second, in comparison to Bryant and Trabasso's results, our decreased learning criterion seems to have worsened the performance only on the learnt pairs (Table 2). This fact does not fit very well with the Bryant and Trabasso idea that it is because memory deficits were avoided in their experiment that the young children succeeded, for under this hypothesis, reducing the learning criterion should particularly have affected the non-adjacent, transitive pairs in our experiment.

Both these aspects of our data indicate that the method used by the children does not depend very much on remembering the learnt pairs, a fact which is difficult to understand if the children are making transitive inferences. As in addition the children executed the task with surprising ease, we felt that we might do well to search for the existence of possibly simpler alternative strategies before claiming that the observed behaviour was the result of a transitive inference independent of the memory of adjacent pairs.

Our subsequent experiments were designed to test whether alternative strategies related to the order of learning of adjacent pairs or the grouping of the sticks by "labels"

might explain the results. We used children between 3 yr 10 month and 4 yr 6 month (mean 4 yr 3 month) being slightly younger than the 4 yr 5 month of Bryant and Trabasso's youngest age group. We retained the criterion of learning used in our experiment I.

It is possible that, as Bryant and Trabasso presented sticks in ascending or descending order, the children in their experiment remembered the order of occurrence of new sticks seen in the sequence of presentation. Thus every new stick seen would be added to a list such as "blue, black, red, etc. . .". In the test phase of the experiment, the child only needs to check which of the two sticks he is shown occurs first in the list. In the case of decreasing presentation, this will be the biggest stick, and in the case of increasing presentation, it will be the smallest.

In experiment II we modified the technique used before so that during all phases of the training the pairs of sticks were presented in random rather than ascending or descending order, for example EC DE AB CE, or AB CD DE BC.

The results of the test are shown in Table 3. There is clearly no evidence that the children do worse in this "disorder condition". This failure to diminish performance in the test goes against the idea that the children are remembering the order of presentation of the sticks.

Table 3 Presentation in Random Order of Forty Children (Experiment II) aged 3 yr 10 month to 4 yr 6 month (Mean Age 4 yr 3 month)

Correct choices A > B > C > D > E (%)				
	B	C	D	E
A	73	83	87	92
B		88	81	90
C			84	96
D				94

All scores significantly different from chance at 0.001 level (see Table 1).

Four responses per pair per child.

On the other hand, the data do not seem to undermine the claim that the children are able to make transitive inferences in the conditions of the Bryant and Trabasso experiment. In a control experiment, however, we found that, in contrast to children, adults do considerably worse in the disorder condition than in the order condition (Table 4). We can conclude that children implement transitivity differently, and sometimes better than adults. Alternatively, and more consistent with the data presented below, we can suppose that the children in these experiments were not using transitivity at all.

The hypothesis of the 'labelling strategy' seems to be complicated at first sight, but is in fact simple, being derived from the idea that in young children the notion of size is absolute rather than relative. It is proposed that the child does the following three things during the training phase of the experiment. First he remembers each pair as a "situation" in which he can make the correct judgment: when confronted with rods A and B together, he says A is bigger and B smaller. When confronted with B and C together he says that B is bigger and C smaller, and so on. He makes no effort to combine these individual situations, as to him they do not conflict.

Second, he attaches absolute labels to the rods: if in a given situation a rod is longer, it gets the label "big" if it is smaller, it gets the label "small". Rods which can be both big and small retain no useful label. Thus, at the end of the training phase, the rod A has the label "big", and the rod E has the label "small", while the rest are "nonentities".

The third hypothesis is that if a rod has occurred in a situation with a rod that has a given label, it may acquire the same label. Thus the rods B and D are not always "nonentities", as B can become "big" and D can become "small" by virtue of having been presented with A or E.

What the child retains from the training phase of the experiment is therefore a memory of the correct answer to each pair of adjacent sticks; a "labelling" in which stick A is considered "big", stick E is "small"; and from the third hypothesis one or both of the following: that stick B is also "big" (a) and/or that stick D is also "small" (b).

Summarising the result of this procedure the sticks fall into three groups: the "big", the "small", and the "nonentities". Depending on what version of the third hypothesis is used the sticks will be differently distributed in the groups. When stick B is also "big" (a) the grouping will be "big" AB, "nonentities" OD, "small" E; when stick D is also "small" (b) it will be "big" A, "nonentities" BC, and "small" DE; and with both (a+b) it will be "big" AB, "nonentities" C, and "small" DE respectively.

Given any two sticks, the child can use one of two methods to make the correct response. If they are adjacent, he needs only remember the response he was taught to make on that pair. If they are not adjacent, at least one of them will belong to the big group, or to the small group, and so will be considered bigger, or smaller, than the other stick.

Clearly this "labelling" strategy cannot be considered as transitivity. Yet it is perfectly consistent with all the data assembled above. Indeed certain aspects of the experiments discussed above are better dealt with than if we assume that the children are making transitive inferences.

In particular, because of the reduced training given in experiment I, during the test the children may have had difficulty remembering the comparisons they were taught, and may thus have resorted to using labels instead. As, by virtue of the third hypothesis, two adjacent sticks may in fact have the same labels, confusions must have arisen on these pairs. This explains the fact that whereas reducing the training criterion did not affect the performance on unlearned, transitive pairs, that on learnt pairs was diminished compared with the Bryant and Trabasso results.

The idea that confusions can arise on pairs having the same label enables us to determine whether hypothesis a, b or a+b is more common. Looking over the success rate of all pairs over all types of presentation we find that grouping seems to occur mainly according to hypothesis a, that is AB, OD and E. Thus AE, BE, CE and DE (comparisons with the smallest stick) fall into a group having the highest scores. AC, AD, BD and BC (comparisons with "nonentities") have lower scores. The comparison AB between the two "big" sticks has the lowest score of all. It will be noted that the same grouping, with the smallest stick standing alone, recurs in all our experiments.

An essential aspect of the "labelling" strategy described above is that we must make the assumption that during the test the child is sometimes content to take his decisions on the basis of the label of only one of the sticks, the other one being a "nonentity", which is neither "big" nor "small". We made use of this fact in our third experiment, which was designed to determine if there was actually positive evidence that the children were using the "labelling" strategy or some derivative of it.

Table 4 Comparison of Adults' and Children's Performance in Ordered and Disordered Presentations

Total number of correct answers in the test (maximum score=40)					
	Ten subjects in disordered presentation		Ten subjects in ordered presentation		Significance of difference between the two types of presentation *
	Median	IQR	Median	IQR	
Random adults	25	5	40	0	0.05
Children in experiments I and II	34.5	2	35.5	2	n.s.

* By χ^2 test of the generalized median.
IQR. Interquartile range

Table 5 Ten Children (Experiment III) aged 3 yr 10 month to 4 yr 4 month (Mean Age 4 yr 1 month)

	B	C	D	E
A	72	88	92	89
B		60	70	80
C			46	80
D				89

Four responses per pair per child. % "correct" choice relative to the hypothetical ordering $A > B > C > D > E$.

Table 6 Percentage Scores given Relative to the Hypothetical Ordering $A > B > C > D$ of Thirty Children aged 3 yr 10 month to 4 yr 6 month (Mean Age 4 yr 2 month) (Experiment IV)

Pair	Score	Predicted score according to labelling hypothesis	Number of children making 7/8 or 8/8 choices so that both $A > D$ and $B < C$	Mixed case †	Predicted score according to ordering hypothesis				Number of children making 7/8 or 8/8 choices such that both $C > B$ and $D > A$
					Case $A > B > C > D$	Number of children making 7/8 or 8/8 choices so that both $A > D$ and $B < C$	Case $C > D > A > B$		
$A > B$	88 *	100	15	100	100	None	100		None
$A > C$	52	50		50	100		0		
$A > D$	85 *	100		50	100		0		
$B > C$	27 *	0		50	100		0		
$B > D$	50	50		50	100		0		
$C > D$	87 *	100		100	100		100		

* Significantly different from chance at 0.001 (see Table 1).

† Combining random choice of $A > B > C > D$ and $C > D > A > B$ for all thirty children.

In this third experiment, we proceeded as before, except we simply left stick C (always a "nonentity") out of the training phase, and trained the children on pairs AB, BD and DE. But in the test stage, the middle stick was used exactly as in the preceding experiments.

We predicted that stick C, never having been seen before, would fall into the group of "nonentities". Our prediction was confirmed. The children showed no surprise when suddenly confronted with stick C in the test, and they gave the responses shown in Table 5.

The labelling idea is clearly compatible with the results. Stick C is generally inserted between sticks A and E. Its position is slightly more often confused with D than with B, suggesting that after the training with four sticks, the grouping ABDE was preponderant.

It is important to note, that, as they contain pairs which are logically undecidable, this and the following experiment cannot give direct evidence against the hypothesis that the children possess the idea of transitivity. But inasmuch as the results of these experiments go against a hypothesis which might be considered to be derived from or a prerequisite for the idea of transitivity, that is to say the ordering hypothesis, and inasmuch as they do support the labelling hypothesis in general, it becomes plausible that the labelling hypothesis might also be used in the transitivity experiments I and II.

As a further test of the "labelling" hypothesis, we performed an experiment with only four sticks (experiment IV), in which the training was considerably simplified. Only two pairs of sticks were presented, namely AB and CD. Using this condition the children know that A is bigger than B, and that C is bigger than D, but they have no way of knowing the relation between A and C, or between B and C.

On the "labelling" hypothesis, as both A and C have the same label ("big"), and as both B and D are "small", we would always expect the child to consider $A > D$ and $B < C$.

Alternatively, one might expect that a young child possessing the notion of transitivity or using any kind of "ordering method" would impose an order on a set of sticks even when there is insufficient information to know the correct order. Thus in this experiment the most obvious thing

for him to assume is either $A > B > C > D$ or else that $C > D > A > B$. Under this hypothesis then, and in contrast to the "labelling" hypothesis, if the child chooses $A > D$, he should make $B < C$.

The results of the experiment are shown in Table 6. It is seen that the tendency is to consider $A > D$ and $B < C$, thus confirming the prediction made according to the labelling hypothesis.

Because the young child is unable to say directly what he knows, the researcher studying abstract ideas is forced to evaluate the child's ability indirectly by means of the child's

behaviour. This means that it is difficult for any single experiment to bring unequivocal evidence for the existence or absence of a given cognitive capacity. Just as failure can always be attributed to difficulties such as with material or memory overload, success can always be brought about by the use of some kind of material-orientated heuristic which happens to work in the given situation.

In their experiment to show up transitivity in young children, Bryant and Trabasso used an ingenious method to obviate mnemonic and manipulation difficulties. But they omitted to check that success in their experiment could not be brought about by other strategies.

In our experiments we have found that Bryant and Trabasso's idea that their children succeeded because a memory difficulty had been overcome is not entirely convincing. Our results also indicate that a "labelling" strategy in which no idea of relative length or order is needed cannot be excluded as a possible heuristic in the Bryant and Trabasso task. Indeed, predictions made according to this hypothesis are more consistent with the data than the idea that the children are making transitive inferences.

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BOOK REVIEWS

Pigmentation and Evolution

The Evolution of Melanism: The Study of a Recurring Necessity, with Special Reference to Industrial Melanism in the Lepidoptera. By Bernard Kettlewell. Pp. xxiv+423. (Clarendon: Oxford; Oxford University: London, August 1973.) £10.25.

H. B. D. KETTLEWELL is the world authority on the experimental study of melanism in the Lepidoptera. It was he who pioneered this subject, and much of the subsequent field work by others has been based on his original experimental techniques. The publication of this book is therefore quite an event.

The book contains not only an account of many aspects of melanism but also detailed descriptions of the author's massive contribution to our knowledge of the phenomenon in the Lepidoptera. He recounts in detail his ingenious experiments which first demonstrated intensive selective predation by birds on moths, which largely accounts for the presence of melanics in both industrial and some non-polluted rural areas. Thus, his comparative study shows that melanics can be at an advantage in certain ecological circumstances unassociated with industrialisation, and that identical phenotypes can be advantageous in both industrial and non-industrial conditions. He details his studies into the rare phenomenon of a polymorphism where the melanic is a recessive and not a dominant. The author shows that melanism in the Lepidoptera is a very old phenomenon. This conclusion, coupled with his genetic work on the control of dominance in the peppered moth, leads him to postulate that the present dominance relationships between melanic and non-melanic forms are due to the evolution of dominance in the distant past.

The text of this book makes extremely interesting reading and will fascinate the general reader concerned with the study of microevolution, for there is a great deal of information packed into it. The specialist will, however, find the book quite difficult in places for several reasons. First, there is a number of typographical errors (the largest I have ever seen in a scientific work), some of which are confusing. Second, many of the plates and figures have quite inadequate legends, nor are they properly explained in the main body of the book. Third, the most ap-

propriate references are frequently not given, and the text does not agree with the appendices. These criticisms can be illustrated by a selection of examples. Thus the symbols < and > are confused in many places. On page 181 *Xylophasia exilis* is said to be found in many areas over 100 feet on the north Scottish mainland. I wonder if this is a misprint for 1,000 feet. On pages 316-317 it is stated that 94% of the gene-complex of a hybrid brood, described as an F₁ between British and Canadian stock, must be of Canadian origin. This is clearly wrong, surely it is the fourth backcross. On plate 15.1, No. 6, the butterfly is said to be a female but is clearly a male. Perhaps one of the most inadequate legends to a figure is to be found on page 204. The figure is entirely useless since we are not told how it was constructed, for example with respect to the daily survival rate used.

At the top of page 136 Kettlewell refers to the cline in the frequency of melanics of the peppered moth from Liverpool into North Wales and cites a paper by Clarke and myself (1963), whereas the most up-to-date reference to this study is 1966. The author certainly knows of the latter paper since it is referred to at the bottom of the same page but in a different connection. However, he does not refer to these extensive data in appendix C when he is recording the frequency of melanics in various localities in Britain. There is a number of serious discrepancies between data quoted in the text and those given in appendices B and C. Consequently one does not know which values to believe. Furthermore, when discussing exceptionally high frequencies of melanics in *Gonodontis bidentata* it is not clear why the author picked Leeds, since a paper by Askew *et al.* (1971), which appears in the bibliography, shows that it reaches an even higher frequency in parts of Manchester. Unfortunately in appendix B it is not made clear that the actual location within a town is important when considering this species, and Manchester is listed as having a frequency of melanics of 55.4%, and no reference is made to the more accurate data of Askew *et al.*

The author gives an extensive bibliography. It would, however, help the reader if he indicated which entries were cited in the text and which were given as additional reading.

Perhaps the most serious criticisms

of the book stem from two remarks in the preface. First, the author says: "Designs of experiments laid down in advance from armchairs by biometricians, without intimate knowledge of the intricacies in the field, frequently failed." However, some statistical advice might on occasion have been useful. Thus when one examines the experiment mentioned on page 283 in which a monomorphic colony of *Panaxia dominula* f. *bimacula* was deliberately established, one finds that two of the avowed four objectives of the experiment—(1) to compare the behaviour of the *bimacula* and the *typica* forms, and (2) to study possible differences in the reaction of the predators to these two forms—cannot be achieved by the design of the experiment. This is obvious since the genetic constitution of the colony will be unique. Consequently any conclusions about the comparative behaviour of the two forms based on the *monomorphic colony* will be invalid, since both forms with a similar genetic background are not available to study. Furthermore, the reaction of the predators could only be observed with respect to one of the forms, the other being absent.

The second difficulty arises from the author's philosophy when he says: "Nor can I see any advantage in re-writing the techniques and results of experiments which I consider were adequately presented at an earlier date". This attitude has led him into serious difficulties. The figure on page 145 purports to be the relationship between the frequencies of *insularia* plotted against *carbonaria* frequencies. It is clear that this cannot be so, since populations with 90% or more *carbonaria* sometimes have frequencies of *insularia* in excess of 40% in the diagram. In the body of the text we are told that the curve refers to the estimated gene frequencies of the two forms. But this also cannot be right since on page 142 the author states that the two forms are, on occasion, controlled by allelomorphs of the same locus. It transpires that the diagram has been taken from Kettlewell's 1958 paper, where it was assumed that the two loci were independent. Since the text has not been changed from the original paper in order to take this into account, this and the figure are useless, even if the conclusions by some happy chance may be correct. Incidentally, we are told that the diagram is

based on the data from appendix C, but in fact it ignores all the data collected since 1956. The figure showing the British distribution of melanics, page 135, has also been lifted bodily from the same paper and has not been updated, thus it loses a great deal of its value.

Despite these serious criticisms, and many more, the volume is clearly essential reading for students of microevolution. One of its very great merits is the large number of speculative conclusions which have never been published before, and which will be a fruitful source of future experiments for many years to come. If the author had taken a great deal more trouble with the book and the publishers had made sure the plates were inserted in the right places (they have not in my copy), this book, instead of being a very interesting and useful volume, would have been a brilliant one.

P. M. SHEPPARD

Estimating Animals

The Estimation of Animal Abundance and Related Parameters. By G. A. F. Seber. Pp. xii+56. (Griffin: London, May 1973.) £12.

OFTEN a first problem in ecology is to devise a census technique. Rarely are direct absolute counts possible and recourse must be made to sampling methods. Many of these have been derived by statisticians and mathematicians and they answer the purpose just so long as the simplifying assumptions on which they are based are applicable. This book, written by an authority in statistics (indeed the author is Professor of Statistics at Auckland University), brings together the various mathematical techniques for estimating animal numbers and such related parameters as birth, mortality and migration rates. It is certainly useful to have all these techniques presented as a reference text which adopts a standardised notation, defined in a preliminary chapter, but with this somewhat esoteric content the book is rather expensive. Its value to a practising ecologist must depend on its accuracy, and its completeness, and perhaps also on any critical discussion of the validity and scope of the techniques mentioned.

On the first point the book certainly scores, for the field has been surveyed comprehensively and well. Each major topic, for example, the chapter dealing with "mark releases before the sampling period in open populations", is broken down to such categories as "single release: instantaneous sampling" or "single release and continuous sampling: mortality estimates" and under this last head maximum-likelihood and regression estimates are considered. In this way, and throughout the book, the final

classification usually resolves into a particular mathematical technique defined by equations and followed by one or two worked examples from the literature.

Printers and bad proof reading can make 'hash and blotty' out of mathematical equations and symbols—indeed, some of the original published methods have appeared with irritating errors such as wrong signs. At a quick check I have found no errors in the formulae but my search has not been exhaustive.

On the third point, the book is a bit disappointing, for it offers no real discussion of the validity of the underlying biological assumptions. In capture-recapture studies it is invariably a necessary assumption that every animal in the population, whether marked or unmarked, has the same probability of being caught in the i -th sample, assuming it to be alive. Real animals rarely satisfy such premises. In fact, it might be suggested that the essence of survival has been the evolution of predictive mechanisms, of information exchange through communal behaviour, of social hierarchies which restrict movement, indeed of a host of conventions which serve to remove any element of chance and therefore confound our simple premises that individuals can be assumed to behave randomly. Perhaps we need some new approaches. In the meanwhile, this book will serve as a helpful reference work for numerate experts.

R. K. MURTON

Statistics in Medicine

Causal Thinking in the Health Sciences: Concepts and Strategies of Epidemiology. By Mervyn Susser. Pp. xviii+181. (Oxford University: London and New York, August 1973.) £2.20.

ONLY the first part of the title of this book appears on the cover, on the fly-leaf, and on each page. This gives a most misleading impression. It leads one to expect a proposal of some novel mode of reasoning, or perhaps a polemic on the inadequacy of current modes of reasoning, about medical practice. Indeed, I missed the title page and read with initial prejudice and with growing surprise. For in fact the book is a systematic examination of epidemiological methods in medicine, that is, of using statistical data to establish the existence of hazards to health and the means of preventing them. This is the discipline that has to its credit the discovery of the means of eliminating cholera before the cholera vibrio was known; the discovery that most bronchial cancer, and most chronic respiratory disease, is linked in some as yet unknown way to the smoking of cigarettes and can be avoided by avoiding such smoking; the discovery

that asbestos is capable of causing, by as yet unknown means, cancers of the mesothelial layers of the lung and other viscera.

Epidemiology has also discovered, however, associations between the softness of domestic water supplies and mortality from ischaemic heart disease, and between potato blight and births of children with spina bifida. Whether these associations reflect causal links is still a matter for dispute, and conflicting evidence has been produced. Professor Susser's concern is with the nature of epidemiological evidence, its classification into types, and the discovery of means by which direct causal links can be distinguished from indirect ones and from associations with no causal element at all.

The first six chapters provide an introduction to epidemiology and to the complex interplay between the environment and the population inhabiting it. The discussion is general, though cogent examples are given, often in the form of what the author calls "exhibits"—tabular or graphical data displayed as if on a wall-board. The development is clear, but heavy going and handicapped by technical terms of low mnemonic value which are introduced as new factors are recognised to enter the epidemiological situation. One finds, and can in part translate with the aid of the index, sentences such as "The characteristic that distinguishes the component variable from other control variables is its integration, by definition or implication, with the global independent variable under study". Mercifully they are uncommon.

In the remaining five chapters the strategies available to the epidemiologist to elucidate complex associations are examined systematically. These chapters are stimulating and thought provoking, and they succeed to a great extent in reducing to order the variety of difficulties that beset this process. No general principles emerge for recognising the disturbing factors that may be present in a particular case, and the student must learn by analogy to try to guess what they may be by noting what in other cases they have been. Once again, however, the naming of these factors is unhelpful: "When a moderator variable is introduced into an analysis, and reveals interaction, the process is called specification". Incidentally, interaction is here defined as the difference between the mean effects of one factor when another is present or absent. This is twice the size of the interaction according to the conventional statistical definition.

The book can be strongly recommended, not only to epidemiologists, but also to those interested in the findings of epidemiology. It represents a major advance in the process of establishing

standards of rigour for epidemiological arguments, and should generate much fruitful debate. I would, for instance, argue the wrongness of the statement "In the social and biological world, the more general and mathematical a formulation the less it is likely to represent the parochial realities of our concern". Are we really more interested in predicting a local epidemic with precision than with giving insights into the process of its spread? P. D. OLDHAM

Skye is Only the Start

Past and Present Vegetation of the Isle of Skye: a Palaeoecological Study. By H. J. B. Birks. Pp. xi+415. (Cambridge University: London, June 1973.) £13.50; \$39.50.

THIS book is without precedent in the history of plant ecological literature both in its intensive examination of the flora of a relatively small area and in its attempt to marry palaeoecological studies with a survey of modern flora. Although its title might suggest a highly specialised work of limited appeal, the book contains several sections which are of considerable relevance to many ecological fields.

There are two main sections to the work, the first being a detailed survey of the present vegetation of the Isle of Skye and the second dealing with the author's palaeoecological investigations of certain sediments on the island. The first section occupies more than half of the book, mainly as a result of ninety-six pages of phytosociological tables included within it. These tables document an extensive survey of the island's vegetation carried out by recording 551 four-metre-square quadrats, selected subjectively to ensure complete coverage of the island's diverse habitat types. The results are arranged in tables resembling those of the Braun Blanquet continental system of phytosociology, differing only in the absence of sociability indices. The classification and nomenclature of "vegetational units" also follow the continental system.

Many British ecologists will object to the use of subjective techniques and also the application of the continental 'pigeonhole' philosophy in classifying stands. One must, however, acknowledge the efficiency of these methods for primary vegetational survey. Continental phytosociologists may feel that some of their carefully defined association binomials have been applied a little loosely to some of the very distinctive, oceanic plant communities of Skye. The author has declined to erect new associations on the grounds that too little is known of the fidelity of species within the vegetational units he has recognised. Without such a know-

ledge, however, he may have been unwise in assigning some of them to existing associations mainly described from the continent.

The palaeoecological section of the book contains a very valuable chapter on pollen identification. There are also extremely useful data on surface pollen spectra from different vegetational types which aid the interpretation of the fossil pollen assemblages. Pollen analyses are given for sediments from five sites on Skye which were chosen to provide representative examples of vegetational history in a region of diverse topography and geology. The diagrams are zoned on a local assemblage zone basis, but are interpreted as representing the classical late Devensian sequence, including the interstadial phase (Allerød). Undoubtedly some people will question this interpretation. *Betula* pollen is present in very low quantities in the basal sediments and does not provide clear evidence upon which zonation can be based, except possibly at Loch Meodal. *Juniperus*, on the other hand, does exhibit the expected double peak associated with the complete late Devensian sequence. My feeling is that Birks is probably correct in his interpretation; however, it is regrettable that he does not possess more radiocarbon dates from lower (interstadial) levels. At present the temporal correlation chart (Fig. 27, page 352), which summarises Birks' conclusions, must be regarded as speculative.

This is a remarkable book describing the results of a great deal of painstaking and accurate work. It is a volume which will undoubtedly have a profound influence upon the future development of Quaternary plant ecology in the British Isles.

PETER D. MOORE

Urchins and Cucumbers

Experimental Embryology of Echinoderms. By Sven Hörstadius. Pp. 192. (Oxford University: London; Clarendon: Oxford, September 1973.) £5.

For more than forty years experimental embryologists have recognised Sven Hörstadius as a master. From time to time he has displayed his outstanding skills on other material, but the analysis of sea urchin development has been his major and continuing interest. He now offers a historical review, informed by a lifetime's familiarity, and ruthlessly down to earth in its approach. Starfish, sea lilies and sea cucumbers have been less conspicuous in experimental work, but are appropriately mentioned.

Hörstadius deliberately avoids any detailed consideration of a number of important fields—fertilisation and the molecular biology of eggs and embryos, for example—in order to concentrate upon his main theme. This is experi-

mental morphology as investigated by the classical manipulative techniques of isolation and transplantation, and 'simple' chemical treatments. The story is well known in outline, and is very impressive. It is useful to have it brought up to date in so authoritative a way.

The example of Driesch may have discouraged later echinoderm embryologists from grandiose speculation, but it is a pity that Hörstadius is so very self controlled. It would have been of interest to know more of his views, however tentative, on the general issues that this work raises. Even the double gradient which has been so helpful in interpreting experimental results must arise, must be maintained, and must influence the expression of genetic information. To understand how would be of universal value for developmental biology. Hörstadius's questions are usually less general. It is wholly characteristic that his book should end with one that smacks more of the laboratory than the seminar. An experiment is briefly described. The expected result is not obtained. "Instead, the upper half moved down along the lower partner until the endodermal regions fused. What kind of reaction and what forces caused this strange migration?"

D. R. NEWTH

More Quanta

Theoretical Physics: an Advanced Text. Volume 3: Quantum Mechanics. By Benjamin G. Levich, V. A. Myamin, and Yu A. Vdovin. Translated. Pp. xx+621. (North-Holland: Amsterdam and London, 1973.) Dfl. 120; \$37.50.

THE writing of a book on Quantum Mechanics, at the present time, requires a certain temerity on the part of the author. Only a messianic belief in the originality and individuality of one's approach could justify the adding of yet another volume to the already overcrowded shelves.

The present volume is neither original nor particularly individual, and its sole *raison d'être* seems to lie in the unwarranted conviction that every course on Theoretical Physics should possess its own volume on Quantum Mechanics.

One of the basic problems is to try to identify the audience it might serve. It is much too advanced to be used as an introductory text for undergraduates, even for those specialising in theoretical physics, and it does not match, say, Landau and Lifshitz for excitement and power, as an advanced treatment.

The subject matter is rather standard, with the exception of the last chapter entitled "Fundamentals of the Theory of Elementary Particles", where an interesting attempt is made to introduce the reader to quite advanced ideas which are right in the forefront of present day

research. It makes fascinating reading. In the foreword, we are also promised detailed applications to solid-state theory, but these have failed to materialise.

Some topics are rather nicely handled. The standard treatment of potential wells and barriers is enhanced by the study of some of the numerical magnitudes of the effects. The use of integral equations and Green's functions is very clearly discussed, though the presentation is somewhat lacking in motivation. The treatment of the time-energy uncertainty relations, as is traditional in the Russian school, is good. The Periodic Table and Molecular Spectra receive enough discussion to give one a real flavour for what is involved. The treatment of Coulomb Scattering begins with the case of the Screened Coulomb Potential. This leads to a natural introduction to the concept of the atomic form factor, and also avoids the mathematical and conceptual complexities associated with the pure Coulomb force. The seemingly mysterious agreement between the quantum and classical calculations of the Rutherford formula, usually not commented upon, is explained. The derivation of the classical limit of scattering theory is a noteworthy inclusion. The treatment of symmetry properties, in particular of the group $SU(2)$, is unusually good, in that it uses basic Lie Group methods, applicable to more general cases, and does not capitalise on the special and rather atypical properties of $SU(2)$ itself.

On the negative side it has to be said that the description of "wave-particle duality" is clumsy and that the whole introductory chapter, which is wide ranging and far from simple, would be incomprehensible to a newcomer to the subject. Matrix algebra is discussed in detail, yet for an understanding of the δ function one must turn to Volume 1 of the course—a strange choice of priorities. The Hamilton-Jacobi equation is introduced, yet inadequately explained. There is a long discussion of α decay and of the sensitivity of barrier effects to the energy, yet no numerical estimate to illustrate it. The derivation of degenerate perturbation theory, always a tricky question, is quite unclear, and there is in general far too little illustration of the use of perturbation theory. A fair-sized portion of the book is devoted to Relativistic Quantum Mechanics (Dirac equation, Weak and Strong interactions, Feynman diagrams). Here one has the feeling that the reader will pick up only a very superficial idea of what is involved.

The reader will be confused, after having being led through the seemingly general proof in Section 73 that the dipole moment of an atom is zero, to learn somewhat later, and without explanation, that "As distinct from

atoms, molecules may have a mean dipole moment".

The translation sometimes leaves much to be desired. "Causality" and "determinism" are confused, as are "picture" and "representation"; "measurement" is used instead of "dimension" and "rank" of a matrix for its "dimension". Some phrases are particularly outlandish: "We digress from other quantities . . ."; "The trace of a scalar is equal to its quadrupole value"; "The reaction $p + \gamma \rightarrow n + \pi^+$ representing the elementary act of the nuclear photoeffect was observed"; and so on.

Also the notation is occasionally non-standard, and it is inexcusable that no effort was made, in translating the volume, to comply with Western usage. Examples are: $\{ \}$ for the commutator bracket, R_x for the operator generating displacements along the X axis, and $*$ used sometimes as hermitian conjugate and sometimes as complex conjugate.

By and large this is not an attractive book. It is neither fish nor fowl, and aside from the rather nice treatment of a few selected topics, it is hard to see to whom it may be recommended as a whole.

E. LEADER

Art of Bonding

The Shape and Structure of Molecules. By C. A. Coulson. Pp. 85. (Clarendon: Oxford; Oxford University: London, June 1973.) £2.75 boards; £1.50 paper.

THE aim of this book is "to show how a few quite simple ideas, not particularly abstruse or mathematical, have been able to rationalise a large part of structural chemistry". The fundamental concept of localised bonds, with their characteristic energies and electron distributions, is established for diatomic molecules, using both the Heitler-London and the molecular orbital approach. The concept of hybridisation leads to a discussion of polyatomic molecules, which is followed by a short survey of valence rules for elements in the main groups of the periodic table. The final chapter gives a very brief discussion of delocalised bonds.

A book of this length cannot do more than introduce so vast and subtle a subject. The understanding of bonding is an art at least as much as a science, and only experience can teach us which approximate or qualitative treatments are useful and what is the likely range of their validity—as tested, for example, by predicting both the correct shape and stability of molecules and the correct electronic distribution obtained from X-ray scattering. Until one has digested the results of applying various bonding theories to known properties of a wide range of molecules and crystals, one cannot apply them with any confidence

to the unknown. For this purpose a much larger book is needed, which would discuss critically not only many more applications of the theory given here, but also other treatments of bonding, such as that of Sidgwick, Powell, Nyholm and Gillespie. Recognising this, the present book ends with useful suggestions for further reading.

To sum up, this book can be recommended as an introduction to the art of bonding theory, outlining the particular approach of a master practitioner both of that art and of the art of exposition.

T. H. K. BARRON

Isotopes in the World

Stable Isotope Geochemistry. By Jochn Hoefs. (Minerals, Rocks, and Inorganic Materials: Monograph Series of Theoretical and Experimental Studies, vol. 9.) Pp. ix+140. (Springer-Verlag: Berlin, New York, 1973.) 39 DM; \$14.50.

THIS small volume, which is essentially an up to date review of the most significant contributions to stable isotope geochemistry over the last ten years or so, is divided into three main sections. The first is an introduction which briefly covers some background material relating to isotopes in general, including isotope effects and fractionation processes, mass spectrometry, sample handling, and standards. This is followed by a more detailed discussion of isolation and preparation techniques, fractionation mechanisms, and the standards appropriate to the major elements studied in stable isotope geochemistry: H, C, O and S. Other less studied elements such as Se, B, N, Si, Cl, Br, Li, K, Mg and Ca are briefly mentioned. Finally, in the third and major section, a discussion is given of the variations in stable isotope ratios in various types of geological materials, extraterrestrial samples, the water cycle, and in the atmosphere and biosphere.

Overall the text is easy to follow, largely as a result of the crisp style and of the economy of words, which allow the significant contributions in a comprehensive bibliography of about 500 references to be covered in a relatively short space.

There are only a few typographical errors, for example in the equation on page 35. My only other criticism is that the author has omitted to mention one very active area in stable isotope geochemistry: the lunar rare gas isotope studies which have contributed much to the understanding of the dynamic processes which have occurred on the Moon's surface.

This book should provide invaluable reference work for many who teach and do research in geochemistry.

T. D. M. M. M.

CORRESPONDENCE

Television

SIR,—It is a relief to discover that *Nature* is beginning to watch the television screen with other than a conservative or jaundiced eye. For the most part, your recent writers have understood the weaknesses, strengths, and technical limitations of the medium. Nevertheless, I suspect that some critics are piqued that the programmes are not wholly satisfying to professors of genetics or readers in physics. I feel they might be unaware of the esoteric nature of the group to which they belong. Science programmes reach a narrow band of the potential audience, but this is vast compared with that touched by any other medium which vulgarises science. Television is laical. It is perfectly possible to use it to put across esoteric ideas in an esoteric fashion; however, to do so would be an uneconomic use of the medium. There are better ways of communicating complicated concepts.

In the past, views have been expressed that science misrepresented on television programmes will distort the public's understanding of the function and aims of scientists. This might be so. But it was worrying to see the boot on the other foot in the recent BBC Controversy programme "Soviet Scientists". Elderly members of the scientific establishment shamelessly (or blindly) manipulated a programme into a piece of propaganda. On that showing, the BBC and its attempts at political impartiality and objectivity has more to fear from science than scientists have from television.

Yours faithfully,

ROBERT REID

22 Colet Gardens,
London W14

Dr Reid was until recently Head of Science and Features at BBC TV.—Ed.

DNA Methylation

SIR,—In the article by Adams¹ two papers^{2,3} from my laboratory have been misquoted. The author¹, in referring to our publications, states: "These latter experiments, however, indicated that the maximum rate of methylation occurred at about the time of gastrulation; . . .". On the contrary, we wrote², in 1965, "From these experiments we cannot conclude that the amount of 5-methylcytosine of DNA at later stages of development changes, because we have

not analysed as yet such parameters as, for example, the amount of DNA synthesised during the incubation period, the pool of methionine and the rate of synthesis of DNA at the stages indicated." And in the 1968 paper³: "No conclusion about quantitative differences of methylation at the different stages can be drawn because no information was collected on the pool of methionine and on the rate of DNA synthesis during the period of incubation with labelled methionine."

Moreover, in the article by Adams¹, reference 4 is a misprint (page 28, column 2, line 8). The right references should be 2 and 7, namely, our two *J. molec. Biol.* papers.

I wish to add a word of caution for the implications derived by Adams from a stated five-fold increase of the ratio of 5-methylcytosine to thymine in the heavy DNA¹. It is essential in all work on methylation of DNA in developing sea urchin embryos to consider the 2,000-fold increase in nuclear DNA, which occurs from fertilisation to the pluteus stage with no change in the total mass, the total nitrogen and the total RNA. An additional factor to be considered in the experiments by Adams¹ is the high toxicity of 5-bromo-2'-deoxyuridine to the embryos.

Yours faithfully,

EDUARDO SCARANO

Professor of Molecular Biology,
International Institute of Genetics and Biophysics,
Via Marconi, 10,
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¹ Adams, R. L. P., *Nature new Biol.*, **244**, 27 (1973).

² Scarano, E., Iaccarino, M., Grippo, P., and Winckelmans, D., *J. molec. Biol.*, **14**, 603 (1965).

³ Grippo, P., Iaccarino, M., Parisi, E., and Scarano, E., *J. molec. Biol.*, **36**, 195 (1968).

Soviet Science

SIR,—I write, not only as a scientist, but also as a member of the Communist Party since my student days in 1932. Many illusions have been shattered during the 40 or so years since then; the process of achieving communist society is much longer and more tortuous than we believed in the 1930s. The way in which this change comes about is conditioned by the specific historical circumstances in each country.

It would take a vivid imagination to conceive of more difficult circumstances than those which the Soviet Union has

had to meet. One has only to consider that there was almost no experience of democratic forms of government on which to build; that the young Soviet Union was invaded by fourteen foreign armies and that it spent years of preparation for war in a hostile world and suffered the unparalleled destruction of the last war, to understand how it is possible for present Soviet attitudes to have developed and become entrenched.

I firmly believe, however, that great efforts should be made in the Soviet Union to open up the ways in which dissent can be expressed and taken into account, and so far, progress in this field has been disappointingly slow. In so far as administrative action is taken to inhibit the expression of dissent, I believe this to be wrong and against the best interests, not only of science, but also of socialism. It may be true that a good scientist is not necessarily a good politician, but that does not diminish his right to express his opinions on political matters.

It is also true that Soviet scientists have a lot to give the world as well as to learn from it but I do not see how they can do so unless they are able freely to take part in conferences and discussions outside the Soviet Union.

Soviet society is developing rapidly and has many splendid achievements to record. But it also has some big problems requiring solution. One of these is the correct handling of dissent, and its solution is crucial to the future of socialism.

I am confident that the problem will be solved as others have been in the past, but one thing is certain, its solution will not be helped, and may well be retarded, by the organisation of a campaign of public protest outside the Soviet Union.

Expression of concern over authenticated cases, provided it is done with understanding and in a spirit of helpfulness and, if I may say so, humility, is more likely to be effective. But there are powerful anti-Soviet propaganda machines waiting for any material which can be used to stir up the cold war and, if we provide ammunition for their campaigns, our efforts will certainly be counter-productive. This is essentially what I attempted to say in the recent BBC Controversy programme "Soviet Scientists".

Yours faithfully,

J. W. JEFFERY

Department of Crystallography,
Birkbeck College,
University of London

Smoking and Pregnancy

SIR,—Your invitation for Dr Yerushalmy to respond to your editorial¹ to the correspondence on smoking during pregnancy arrived a few days after his death. Dr Yerushalmy would have enjoyed contributing to the discussions which centred around the two propositions that he described²: that cigarette smoking acts as an exogenous factor which interferes with the intra-uterine growth and development of the foetus and that smokers may represent a group of people whose reproductive experience would have duplicated the observed pattern whether or not they smoked.

His study on 'Infants with Low Birth Weight Born Before Their Mothers Started to Smoke'³ seems to support the hypothesis that the higher incidence of low-birth-weight infants is due to the smoker, not the smoking. Dr Yerushalmy would probably have made a strong plea, as he did in his paper, to repeat this study on larger samples in other population groups to get a definite verdict on the alternative hypothesis. This could be done by asking large numbers of pregnant women who smoke when they started to smoke, what was the birth weight and the health data of previously born children.

Yours faithfully,

BEA J. VAN DEN BERG

*Child Health and Development Studies,
School of Public Health,
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Oakland, California 94611*

¹Nature, 245, 61 (1973).

²Yerushalmy, J., *Proc. 6th Berkeley Symp. Math. Statistics Probability*, IV, 329 (1972).

³Yerushalmy, J., *Am. J. Obstet. Gynec.*, 112, 2 (1972).

Smoking, Pregnancy and Publicity

SIR,—Professor Burch¹ and Dr Hickey *et al.*² rely heavily on the publications of the late Professor Yerushalmy to criticise my own remarks³. As there still seems to be some confusion about the value of his statistical evidence, I would like to elaborate a little on the points I made in my earlier letter.

First, estimates of the mean difference in birthweight between babies of smokers and non-smokers do, of course, differ, but are all in the 150 to 250 g range, and the exact value for a particular population is not relevant to the argument. Yerushalmy's⁴ test for a shift of 200 g in the mean of the birthweight distributions of babies of smokers is inappropriate.

What he should have tested for was an equivalence of the distributions apart from a shift in mean value, which is estimated from the data and need not be

exactly 200 g. As Dr James⁵ has shown, however, we will still find a reversal in mortality rates in the babies weighing 2,500 g or less, if a given percentage reduction in birthweight due to smoking is assumed, rather than a constant absolute reduction. Moreover, a simple study of the two birthweight distributions, in Yerushalmy's own study for example⁶, reveals quite clearly how an increased mortality among babies of smokers which is associated with a reduction in birthweight will lead to a lower mortality among babies of smokers if only the babies weighing 2,500 g or less are studied. For this reason all of Yerushalmy's analyses of babies weighing 2,500 g or less are irrelevant to the main issue.

Professor Burch quotes Yerushalmy's claim that there is no association between birthweight and age for mothers less than twenty-five years old. There are, however, studies other than Professor Yerushalmy's and with much larger numbers^{7,8} which do show that the proportion of low birthweight babies born to women under twenty is about 20% higher than that for women aged between twenty and twenty-four. Until due allowance is made for this, Yerushalmy's conclusions should not be accepted at their face value.

As Professor Burch observes, I am quite happy to "concede" that the scientific case for a causal relationship is not yet completely conclusive and among other possibilities we need to investigate the 'constitutional' hypothesis. The point at issue, however, is how the available evidence should be assessed, and what publicity should be given to any conclusions.

An impartial observer, it seems to me, would have little doubt that this evidence justifies efforts aimed at persuading pregnant women to stop smoking. Your correspondents, I suggest, have confused this practical, ethical issue with the other problem of scientific proof.

Yours faithfully,

HARVEY GOLDSTEIN

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¹Burch, P. R. J., *Nature*, 246, 177 (1973).

²Hickey, R. J., Boyce, D. E., and Clelland, R. C., *Nature*, 246, 177 (1973).

³Goldstein, H., *Nature*, 245, 467 (1973).

⁴Yerushalmy, J., *Am. J. Obstet. Gynec.*, 114, 571 (1972).

⁵James, W. H., *Nature*, 246, 235 (1973).

⁶Yerushalmy, J., *Am. J. Epidemiol.*, 93, 443 (1971).

⁷Butler, N. R., and Alberman, E. D., *Perinatal Problems* (Livingstone, Edinburgh, 1969).

⁸Chase, H. C., and Byrnes, M. E., *Vital and Health Statistics Series A*, 15 (National Centre for Health Studies, Rockville, Maryland, 1972).

This correspondence is now closed.—Ed.

Literature Citations

SIR,—The transcription of literature citations in scientific articles is rendered unnecessarily tedious by the diversity of arbitrary conventions adopted by different journals. References jotted down for subsequent bibliographical use must be differently transcribed according to the journal in which they are to appear. The differences are matters of form and style as well as of completeness.

We are writing to urge that commissions of editors convene information retrieval specialists, typographers, and some common readers to draw up broadly acceptable conventions that optimise clarity and simplicity in literature citations.

Some specific suggestions are: (1) Each scientific journal should adopt an abbreviation, if necessary, of its original or transliterated title that can be used without confusion anywhere in the scientific literature. The abbreviations of common words such as 'Annual' and 'Comptes Rendues' should be uniform. Local conventions such as the germanic use of lower case for adjectives or special self-reference terms ("This Journal") are to be avoided. (2) The presentation of author's names, initials, publication year, article title and key-words, volume number and pagination should be standardised as to sequence, punctuation and type font. Simplifications should be accomplished by deletions without rearrangement. (3) The title page of articles should bear the complete article reference as it should be cited. Fascicule numbers, issue dates and so on, not normally cited, should appear separately on the page if they serve a function for particular users.

The temporary inconvenience to journal staff in changing habits would be offset, in the long run, by diminished editorial labour in the revision of improperly submitted bibliographies.

Uniformity in these matters would cause little reduction in the marvellous particularity of individual journals and would reduce the burden on authors, readers, and especially secretaries.

Yours faithfully,

MICHAEL YARMOLINSKY

MARIE-JOËLLE HOOGVELD-LEPASTEUR

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Bomb Disposal

SIR,—Disarming and removing explosive devices is dangerous to police and army personnel, and also to the general public. I would like to propose a

method of deactivating bombs, which would considerably reduce this risk.

Liquid nitrogen is relatively safe and easily handled. A bomb sprayed with it for several minutes would be cooled to an extremely low temperature. This would have two effects. First, the battery used to detonate the explosive would become ineffective. I have verified this in the following way. Three brands of dry cell battery (Ever Ready, Winfield, Ray-O-Vac) were cooled to the temperature of liquid nitrogen and tested in a small torch. None of the batteries tested caused the torch to light. When the batteries were allowed to warm up, however, complete efficiency was restored.

Second, the detonator and explosive might reasonably be expected to be unreactive at such low temperatures. A bomb deactivated in this manner could be safely transported to a disposal site in an insulated container partially filled with liquid nitrogen.

Yours faithfully,

GEORGE DAVIDSON

K.R.U.F. Institute of Renal Disease,
Royal Infirmary,
Cardiff

Foraminifera

SIR,—The recent review of Dr J. W. Murray's book¹ by Dr J. R. Haynes

(*Nature*, **245**, 442; 1973) may have confused a number of palaeoecologists by seeming to advocate absolute abundance rather than standardised abundance for the plotting of species distributions. The latter method, now widely employed, is admittedly suspect because it makes the *a priori* assumption that all the foraminifera of an assemblage are competing.

This is not as unsatisfactory, however, as the absolute abundance method which is, of course, much affected by rates of sedimentation. As a result, plots of species using this method are often difficult to distinguish. Standardisation of data reduces this 'background noise' and furthermore enables the calculation of basic ratios (such as benthonic: planktonic or Textulariina: Miliolina: Rotaliina) which are now valuable aids to the palaeoecologist. Obviously, if the approach is biological rather than geological, then the biomass of a species per unit area is the better index.

Yours faithfully,

M. D. BRASIER

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¹ Murray, J. W., *Distribution and Ecology of Living Benthic Foraminiferids* (Heinemann, London, 1973).

As suggested in my review, paucity of data and lack of control of sample material may force us to express species abundances in percentages rather than absolute numbers per unit area of volume of substrate. The desperate inadequacy of this method, however, is shown by the tables in Chapter 1 of Dr Murray's book. Not only does this method impose reciprocal relationships but the percentage figures may show a rise for a particular species between stations when the absolute numbers have fallen and *vice versa*.

At present our understanding of the autecology of foraminifer species is almost nil. Progress towards an evolutionary ecology requires knowledge of the abundance of individual species both in their habitats and when dead as part of the sediment. The variations in numbers and sorting brought about by sedimentary processes which make plots "difficult to distinguish" are precisely what concern geologists and represent the challenge that has to be met before we can properly interpret the geological record. Even where it is thought valuable simply to estimate certain crude ratios these are as easily derived from absolute numbers.

JOHN R. HAYNES

Obituary

Leonard Carmichael

DR LEONARD CARMICHAEL, Secretary of the Smithsonian Institution from 1953–64, died on September 16 in Washington, DC, at the age of 74. He was the National Geographic Society's Vice-President for Research and Exploration at the time of his death.

A distinguished physiological psychologist, Dr Carmichael also achieved renown as a science administrator in the worlds of academia, museology and government. The central unifying interest in his career, which lasted 50 years, was research: his own research and the administration and funding of the research of others.

Dr Carmichael was born on November 9, 1898, in Philadelphia, where his father was a successful physician. In 1917 he entered Tufts University, where his grandfather, Charles Hall Leonard, had for many years been Dean of the Crane Theological School. Here he became interested in zoology and psychology, and later recorded that the

two men whose books had the most influence on him as an undergraduate were the biological ultramechanist Jacques Loeb and the proponent of emergent evolution C. Lloyd Morgan.

Following graduation from Tufts, *summa cum laude*, he began graduate work at Harvard in psychology, developing an interest in a basic biological approach to the science. He later wrote that the accidental finding of a German publication of William Preyer, *Spezielle Physiologie des Embryo, Untersuchungen über die Lebenserscheinungen vor der Geburt*, in the Harvard Library, was a turning point in his life, opening his eyes to a specific area of research in his chosen field of the sensory and neural control of behaviour on which he was to spend many years. "Here at last I saw a way to investigate the topic of major interest to me—the morphological growth of the receptors and nervous system in relation to changes in behaviour as responses are released at various stages during the early ontogenetic development in each mammal

before learning begins, or at least before it becomes important."

He completed his PhD studies and theses and did a year of graduate work at the University of Berlin before beginning his teaching career at Princeton in 1924. Later he taught at Brown, where he gained his first administrative experience as Director of its psychology laboratory, and at Rochester, where he was Dean of the arts and sciences faculty. At Brown, in addition to his teaching and administrative activities, Dr Carmichael began studying the prenatal development of behaviour in mammals. With Dr H. H. Jasper, he developed the electroencephalograph and published in 1935 what is believed to be the first report of such work in America.

In 1938 Dr Carmichael returned to Tufts to become, at 39, one of the youngest presidents in the college's history, but during World War II he was summoned from the campus to fill various posts in Washington. As director of the National Roster of Scien-

tific and Specialised Personnel, he organised the recruiting of scientists to work on the atomic energy and radar projects as well as other research connected to work on the war effort. In this period, Dr Carmichael later said, he spent more than a year of nights on a sleeping car between Boston and Washington. He was also President of the American Psychological Association from 1939-40.

After the war, he was a member and Vice-Chairman of the National Advisory Committee for Aeronautics, the predecessor of the National Aeronautics and Space Administration. President Eisenhower named Dr Carmichael Ambassador Extraordinary when he represented the United States at an international conference at The Hague that wrote a treaty for the protection of cultural property in time of war.

In the course of his academic career, Dr Carmichael published numerous papers on reading and visual fatigue, perceptual assimilation, the development of a kitten's ability to land on its feet, and other aspects of behavioural development related to the functions of the sense organs. Dr Carmichael also collaborated with H. C. Warren on the book *Elements of Human Psychology* (Houghton Mifflin, 1930), which was used as an introductory book for years in many major universities and colleges. They also collaborated on a *Dictionary of Psychology* (Houghton Mifflin, 1934). His later writings include *Basic Psychology*, which he wrote in 1957 to set out his point of view for the educated general reader. *Carmichael's Manual of Child Psychology*, of which he wrote part, went through a third edition in 1970.

On January 1, 1953, Dr Carmichael became Secretary of the Smithsonian, the seventh scientist to direct an institution founded in 1846 with a bequest from the English scientist James Smithsonian, "for the increase and diffusion of knowledge among men". Dr Carmichael, during his 11-year tenure as Secretary, was notably successful in obtaining appropriations from Congress to foster programmes of exhibit modernisation for the Institution's museums. Under his leadership the Institution received \$36 million in Federal funds for a Museum of History and Technology, the Smithsonian's first new building in 50 years.

In 1964, at the age of 65, he insisted on retiring from the Smithsonian. He was then offered the post at the National Geographic Society. There he directed \$1.2 million in annual grants for research into sciences. His projects involved him in many activities, including the work of Dr Louis S. B. Leakey at Olduvai Gorge in Tanzania. He also worked closely with Baroness Jane van Lawick-Goodall, whose pioneering

study of wild chimpanzees broke new ground in the study of animal behaviour. Primatology was long an interest of Dr Carmichael and he had served as President of the International Primatological Congress.

He also served as President of the American Philosophical Society from April 1970-73, and was elected to several scientific organisations abroad, including the Ergonomics Research Society of the Royal Society of Arts in England, and the Société Française de Psychologie. In 1972 the National Academy of Sciences bestowed its highest award, the Hartley Public Welfare Medal, on Dr Carmichael "for eminence in the application of science to the public welfare".

Walter Rudolf Hess

PROFESSOR WALTER RUDOLF HESS, Nobel Laureate for Physiology and Medicine for 1949, the man who brought to light the functional organisation of the diencephalon, died at the age of 92 on August 22, 1973, in his home at Ascona, Switzerland.

In 1917, at the early age of 36, he became Professor of Physiology at the University of Zurich, and in this capacity Director of the Institute of Physiology, a post which he held until his retirement in 1951. He very soon became one of Europe's leading physiologists, and with great drive and energy promoted this branch of science on an international scale. Thus, foreseeing the importance of research on the adaptation of the human body to the conditions of high altitude, he founded in 1931 the international *Hochalpinen Forschungsinstitut Jungfrauoch*. In 1938 he was delegated to organise and preside over the 16th International Congress of Physiological Sciences in Zurich. His strong personality succeeded in keeping the meeting on an entirely scientific base despite the political troubles of that time.

In his scientific work, W. R. Hess combined analytical experimentation with great synthetic power, which enabled him to view the data he obtained within the larger frame of the purposeful organisation of biological phenomena. This was already manifest in his early investigations on the viscosity of blood and general haemodynamics, but even more so in his work regarding the regulation of circulation and of respiration, concepts which were laid down in two monographs in 1930-31. It was this search for the organising principles which led W. R. Hess to begin experimentation with electrical stimulation in the brain stem—the diencephalon, his aim being to explore the autonomic

centres which govern the adaptation of circulation and respiration to the different needs of the organism during rest and work. Hess himself said that he wanted to dedicate only one year to this problem, but the work grew and was extended over twenty-five years to form what is known today as his life's work. He perfected the method of circumscribed stimulation and coagulation of subcortical structures in the unrestrained animal in 1932, and after delimiting the reactive zones in the hypothalamus concerned with regulation of circulation and respiration—results obtained in the anaesthetised animal in 1932—he proceeded to systematically explore the entire diencephalon and adjacent portions of the mesencephalon in the freely-moving awake cat.

Every physiologist is familiar with the film of Hess's cats manifesting autonomic, motor and affective-behaviour effects upon electrical stimulation within the diencephalon. Not so familiar, even today, to many a physiologist are the basic conclusions derived by Hess from his experimental work.

Hess's view of two opposing ergotropic and trophotrophic systems was based on the following observations. Stimulation in the caudal portion of the hypothalamus, besides producing an increase in blood pressure and activation of respiration, also produces a general arousal of the animal which is associated with increased locomotor activity (*Bewegungsdrang*). Stimulation in the predominantly more rostrally lying portions of the hypothalamus and of the septum, besides yielding a decrease of blood pressure and an inhibition of respiration, produces responses which are related to food intake, digestion, excretion and thermoregulation. Thus the former effect—the ergotropic reaction—includes both the autonomic and somatomotor responses which are activated simultaneously during effort, and therefore with expenditure of energy. The latter effect, however, the trophotrophic reaction, subserves restitution of the dispensed energy, and guarantees the balance of the internal environment. A behaviour primarily associated with restitution is sleep, and Hess conceived sleep as a distinct type of behaviour, an active process which is governed by the central nervous system. This view has been confirmed by further research, although the narrow concept of a discrete sleep centre in the thalamus can no longer be upheld today.

The various motor effects of the head and trunk produced from the thalamus and adjacent mesencephalon are related to the regulation of posture. This subcortically organised motor system provides an indispensable support for the execution of voluntary movements by counterbalancing the forces exerted by these movements. Hess called this sys-

tern the ereismic, or supporting, motor system.

The affective-behaviour responses were obtained by Hess from the so-called intermediate zone of the hypothalamus and included the affective defence reaction (rage reaction) culminating in a purposeful and directed attack of giving way to sudden flight. Hess strongly defended the point that the rage reaction produced by electrical stimulation in the intact animal is due to an affective re-tuning of the animal and is therefore distinct from the sham rage observed in the decorticated preparation. This view has been largely confirmed today by electrical stimulation of subcortical structures in man, resulting in emotionally tuned reactions. It is mainly the pioneer work of Hess on affective behaviour which stimulated further research in laboratories throughout the world—research which today provides the neurological basis for psychology.

During his emeritus years, Hess was able to devote all his time to the subject of central representation of behaviour and psychic experience, a problem which had preoccupied him all his life. It may therefore be appropriate to close this short tribute by quoting the closing words of his last book *Psychologie in biologischer Sicht*. "... so ergibt sich die Folgerung, dass der Inhalt des subjektiven Erlebens überhaupt an den Bau des Gehirnes und die Eigenschaften der strukturellen Elemente gebunden ist und dass nur solche Bewusstseinsinhalte entwickelt werden können, welche in der Organisation des Gehirnes ihre Entsprechung haben."

Announcements

Appointments

P. N. R. Usherwood, of the University of Glasgow, has been appointed to the chair of zoology at the University of Nottingham.

Professor Israel Dostrovsky has been elected President of the Weizmann Institute of Science.

International Meetings

January 1-4, The Association for Science Education Annual Meeting (B. Nicholl, Esq., ASE Annual Meeting Secretary, Newman College, Birmingham B32 3NT).

January 2-4, 11th Annual Solid State Physics Conference (Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

January 3-4, 69th Ordinary Meeting of the Society for General Microbiology (Meetings Assistant, Society for General Microbiology, Harvest House, 62 London Road, Reading RG1 5AS).

January 3-4, Molecular Beam Kinetics Group (Professor C. W. Nutt, Department of Chemical Engineering, Heriot-Watt University, Chambers Street, Edinburgh EH1 1HX).

January 4, British Society for the History of Science (The Assistant Secretary, The British Society for the History of Science, 47 Belgrave Square, London SW1X 8QX).

January 5, The Artificial Intelligence and the Simulation of Behaviour Group (Mrs L. Daniels, Department of Computational Logic, 9 Hope Park Square, Meadow Lane, Edinburgh EH8 9NW).

January 7-8, Conference on Technical Aspects of Air Pollution (Mrs Sonia Withers, Centre for Extension Studies, Loughborough University of Technology).

January 7-8, Conference on Research in Mathematics (The Secretary and Registrar, The Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

January 7-8, 7th Public Health Engineering Conference (John Pickford, MSc, ACGI, MICE, FIPHE, University of Technology, Loughborough, Leicestershire LE11 3TU).

January 7-8, The Application of Lasers to the Processing and Examination of Materials (The Meetings Officer of the Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

January 7-9, The Biology and Chemistry of the Crustaceae (The Executive Secretary, Linnean Society of London, Burlington House, Piccadilly, London W1V 0LQ).

January 8, The Annual Histochemistry Meeting of the Royal Microscopical Society (The Administrator, Royal Microscopical Society, Clarendon House, Cornmarket Street, Oxford OX1 3HA).

January 8-10, Biological Clocks and Changes in the Earth's Rotation: Geophysical and Astronomical Consequences (W. F. Mavor, Administrative Assistant, School of Physics, The University, Newcastle upon Tyne NE1 7RU).

January 10, 25th Annual General Meeting of the Institute of Biology (Institute of Biology, 41 Queen's Gate, London SW7 5HU).

January 10-11, Numerical Methods for Constrained Optimisation (The Secretary and Registrar, The Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend-on-Sea, Essex SS1 2JY).

January 14, Measurement and Interpretation of Low Volatiles and Solubilities (The Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1X 8PS).

January 14-18, 5th International Symposium on Magnetic Resonance (International Society of Magnetic Resonance, The Weizmann Institute of Science, Rehovot).

January 14-18, 6th Miami Winter Symposia (Miami Winter Symposia, P.O. Box 906, Biscayne Annex, Miami, Florida 33152, USA).

January 16, The Economics of Natural Resource Depletion (D. W. Pearce, Department of Economics, University of Southampton, Southampton, SO9 5NH).

January 16, The Nature of the Scrapie Agent (Dr J. Barber, Botany Department, Imperial College, London SW7).

January 16-April 10, Winter College on Surface Science (The Deputy Director, International Centre for Theoretical Physics, P.O. Box 586, 1-34100 Trieste).

January 17, 2nd National Conference on Environmental Education (Dr J. Rose, College of Technology, Feilden Street, Blackburn, BB2 1LH, Lancashire).

January 21-23, Hemophilia—Recent Advances in Biochemistry, Physiology, and Therapy (Public Relations, The New York Academy of Sciences, 2 East 63rd Street, New York 10021, USA).

January 23-24, Supramolecular Structure in Solid Polymers (Dr E. F. T. White, Department of Polymer and Fibre Science, University of Manchester Institute of Science and Technology, Sackville Street, Manchester M60 1QD).

January 24, Inaugural Meeting of the United Kingdom Section of the International Solar Energy Society (Dr M. Archer, The Royal Institution, 21, Albemarle Street, London W1X 4BS).

January 29-30, Energy: Alternatives and Risks (Robert R. White, Director, Academy Forum, 2101 Constitution Avenue, N.W., Washington, D.C., 20418).

January 30, Compound Semiconductor Films (The Meetings Officer, The Institute of Physics, 47 Belgrave Square, London SW1X 8QX).

Erratum

In the article "Refining the Earth's Pear Shape" by D. G. King-Hele and G. E. Cook (*Nature*, 246, 86; 1973) which was published before proof corrections could be made, paragraph 1, line 7, should read "... as perigee moved successively north and south ...".

Equation (1) should read:

$$U = (\mu/r) \{ 1 + \sum_{n=2}^{\infty} J_n(R/r)^n P_n(\sin \phi) \}$$

Paragraph 8, line 1, should read "Our previous set of odd zonal harmonics, published in 1969, ...".

In reference 4, 380 should be deleted; in reference 7 delete 381.

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

- Department of Trade and Industry. Report on Research and Development 1972-73. Pp. iii+61. (London: HMSO, 1973.) 65p net. [257]
- British Association for the Advancement of Science. Annual Report, 1972/1973. Pp. 16. (London: British Association for the Advancement of Science, 1973.) [277]
- Annual Report on the Meteorological Office, 1972. Pp. xii+120. (London: HMSO, 1973.) £1 net. [307]
- National Radiological Protection Board. NRPB-R14: A Model for the Evaluation of the Deep Ocean Disposal of Radioactive Waste. By G. A. M. Webb and F. Morley. Pp. 23. (Harwell, Didcot: National Radiological Protection Board, 1973.) [317]
- British Nuclear Fuels Limited. Second Annual Report and Accounts, 1972/1973. Pp. 24. (Risley, Warrington: British Nuclear Limited, 1973.) [18]
- Energy for the Future—Report from the Working Party authorised by the Council of the Institute of Fuel. Pp. viii+28. (London: The Institute of Fuel, 18 Devonshire Street, W1, 1973.) [18]
- Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 274, No. 1241: Numerical Solutions of the Kinematic Dynamo Problem. By D. Gubbins. Pp. 493-521. £1.10; \$3.15. Vol. 274, No. 1242: On the Kinetic Theory of Wave Propagation in Random Media. By M. S. Howe. Pp. 523-549. 95p; \$2.70. Vol. 274, No. 1243: Worldwide Distribution of Geomagnetic Tides. By S. R. C. Malin. Pp. 551-594. £1.60; \$4.50. (London: The Royal Society, 1973.) [178]
- Department of Education and Science. Scientific Research in British Universities and Colleges, 1972-73. Volume 1, Part 1: Physical Sciences, Sections 1-16. Pp. xii+1-434. Volume 1, Part 2: Physical Sciences, Sections 17-36. Pp. 435-1025. £7 net. Volume 2: Biological Sciences. Pp. xxi+809. £6 net. Vol. 3: Social Sciences (Including Government Departments and Other Institutions). Pp. xxx+751. £6 net. (London: HMSO, 1973.) [198]
- Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 274, No. 1244: The Geology of the Bristol Channel Floor. By A. J. Lloyd, R. J. G. Savage, A. H. Stride, and D. T. Donovan. Pp. 595-626+plates 5-7. £1.75; \$4.90. Vol. 274, No. 1245: The Thermodynamics of the Titanium-Oxygen System: an Isothermal Gravimetric Study of the Composition Range Ti₂O₃ to TiO₂ at 1304K. By R. R. Merritt and B. G. Hyde, and, in part, L. A. Bursill and D. K. Philp. Pp. 627-661. £1.40; \$3.90. (London: The Royal Society, 1973.) [198]
- Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 274, No. 1246: Fixed Nuclei Two-Centre Problem in Quantum Mechanics. By J. D. Power. Pp. 663-702. £1.25; \$3.50. Vol. 275, No. 1247: On Wave-Induced Stress in a Ship Executing Symmetric Motions. By R. E. D. Bishop and R. Eatock Taylor. Pp. 1-32. (London: The Royal Society, 1973.) [298]
- Philosophical Transactions of the Royal Society of London. B: Biological Sciences. Vol. 265, No. 872:

- Organization of the Outer Synaptic Layer in the Retina of the Larval Tiger Salamander. By A. Lasnik. Pp. 471-489+plates 47-56. (London: The Royal Society, 1973.) £1.75; \$4.90. [318]
- Natural Environment Research Council. Report of the Council for the period 1 April, 1972-31 March, 1973. Pp. v+168+12 plates. (London: HMSO, 1973.) £1.20 net. [189]
- Proceedings of the Royal Irish Academy. Vol. 73, Section A, No. 11: The Production of Condensation Nuclei by Alpha Radiation. By T. P. Burke and J. A. Scott. Pp. 151-158. 14p. Vol. 73, Section B, No. 11: The Stratigraphy of the Middle and Upper Dalradian Succession Between Glengad Head and Greencastle, Inishowen, Co. Donegal. By J. C. Roberts. Pp. 151-164. 18p. (Dublin: Royal Irish Academy, 1973.) [209]
- The Ridgeway Path. (London: The Countryside Commission, 1973.) Grails. [209]
- The Law of the Sea. By Elizabeth Young and Brian Johnson. (Fabian Research Series, No. 313.) Pp. 48. (London: Fabian Society, 1973.) 50p. [219]
- Sub-Atomic Particles: a New Approach. By Gerald Metcaw. (Review Monograph (Physics), No. 1.) Pp. 12. (Harlow, Essex: Gerald Metcaw, 1973.) 80p; \$2. [219]

Other Countries

- International Atomic Energy Agency. Annual Report, 1 July 1972-30 June 1973. Pp. 75. The Agency's Budget for 1974. Pp. 105. (Vienna: International Atomic Energy Agency, 1973.) [108]
- US Environmental Protection Agency. Action for Environmental Quality. Pp. 20. (Washington, DC: US Environmental Protection Agency, 1973.) [178]
- Pramana: a Journal of Physics. Vol. 1, No. 1, July 1973. Pp. 1-60. Edited by S. Ramaseshan and B. M. Udagankar. Annual subscription rates: Foreign: Institutions and Libraries \$30 or £12; individuals \$20 or £8. Domestic: Institutions and Libraries Rs.75; individuals Rs.25; members of IPA Rs.20; bona fide students Rs.10. Published monthly. (Bangalore: Indian Academy of Sciences, in collaboration with the Indian Physics Association and the Indian National Science Academy.) [218]
- United States Department of the Interior: Geological Survey. Professional Paper 766: Foraminifera of the North Pacific Ocean. By Patsy B. Smith. Pp. iii+27+plates 1-4. (Washington, DC: Government Printing Office, 1973.) 85 cents. [298]
- World Directory of Medical School/Répertoire Mondial des Ecoles de Médecine, 1970. Pp. 147. (Geneva: WHO; London: HMSO, 1973.) 20 Sw. francs; £2.50; \$6. [179]
- Records of the Australian Museum, Vol. 28, No. 15: The Alpheid Shrimp of Australia. Part 1: The Lower Genera. By Dora and Albert H. Banner. Pp. 291-382. (Sydney: The Australian Museum, 1973.) \$4. [179]
- United States Department of the Interior: Geological Survey. Bulletin 1258-E: A New Method for the Determination of Three-Dimensional Deformation Anisotropy in Rock Specimens. By Richard A. Farrow. Pp. iii+12. 25 cents. Bulletin 1372-H: Lower and Middle Tertiary Stratigraphic Units of the San Emigdio and Western Tehachali Mountains, California. By T. H. Nilsen, T. W. Dibblee, Jr., and W. O. Addicott. Pp. iii+23. 35 cents. Bulletin 1376: Some Results of Geochemical Sampling in McCormick County, South Carolina. By Henry Bell, III. Pp. iv+22+plates 1-5. \$1.75. Professional Paper 532: Cenozoic Fossil Mollusks from Western Pacific Islands: Gastropods (Turritellidae Through Strombidae). By Harry S. Ladd. Pp. iv+80+plates 1-20. \$1.50. (Washington, DC: Government Printing Office, 1972 and 1973.) [249]
- Publications du Centre National pour l'Exploitation des Océans (CNEXO). Série: Rapports Scientifiques et Techniques. No. 16: Etude non Linéaire des Ondes Internes dans un Milieu à Deux Couches Fluides sans Rotation. Par Alain G. Cavanie. Pp. 11. No. 17: Etude non Linéaire des Ondes Internes dans un Milieu à Deux Couches Fluides en Rotation. Par Michel Arhan. Pp. 14. (Paris: Centre National pour l'Exploitation des Océans, 1973.) [249]
- Smithsonian Contributions to the Earth Sciences. No. 10: Mineralogy, Mineral Chemistry, and Composition of the Murchison (C2) Meteorite. By Louis H. Fuchs, Edward Olsen and Kenneth J. Jensen. Pp. iii+39. 75 cents. Smithsonian Contributions to Zoology. No. 143: Bibliography and Zoological Taxa of Paul Barsch. By Florence A. Ruhoff. With a Biographical Sketch by Harald A. Rehder. Pp. v+166. \$2.85. No. 151: Revision of Corophiidae and Related Families (Amphipoda). By J. Laurens Barnard. Pp. iv+27. 55 cents. No. 152: Evolution of the Rails of the South Atlantic Islands (Aves: Rallidae). By Storrs L. Olson. Pp. iii+53 (11 plates). 95 cents. No. 153: Western Atlantic Shrimps of the Genus *Solenocera*, with Description of a New Species (Crustacea: Decapoda: Penaeidae). By Isabel Perez Farfante and Harvey R. Bullis, Jr. Pp. 33. 65 cents. (Washington, DC: Smithsonian Institution Press, 1973. For sale by US Government Printing Office.) [259]
- Evolutionary Theory, Vol. 1, No. 1, July 1973. Pp. 1-50. Edited by Isidore Nahi. Subscriptions: All subscriptions from Latin America, Asia, Eastern Europe, and Africa (except South Africa and Rhodesia) \$6. Institutions elsewhere \$15. Individuals elsewhere \$10. Students \$6. Single copies \$4. (Chicago: Evolutionary Theory, Biology Department, 1103 E. 57th Street, The University of Chicago, 1973.) [269]
- Republique Française. Office de la Recherche Scientifique et Technique Outre-Mer. ORSTOM. Travaux et Documents de l'ORSTOM. No. 19: Les Baux du Pacifique Occidental à 170° E entre 20° S et 4° N: Coupes et Cartes par des Oceanographes du Centre ORSTOM de Nouméa. Par H. Rotschi, Ph. Hisard et F. Jarrige. Pp. 113. 24 francs. No. 21: Economie Urbaine d'Antsirabe (Madagascar—1966-1969). Pp. 153. 40 francs. No. 22: Etude Ethnologique et Biocénétique du Peuplement d'Insectes dans un Verger Naturel. Par G. Couturier. Pp. 96. 30 francs. No. 23: Les Plantes Médicinales de la Nouvelle-Calédonie. Par Jean Ragueau. Pp. 139. 42 francs. Mémoire ORSTOM No. 64: Ecologie de *Glossina Palpalis gambiensis* Vanderplank, 1949. (Diptera: Muscidae) en Savane d'Afrique Occidentale. Par A. Chailier. Pp. xvi+274. 100 francs. Faune Tropicale XIX: Les Crévettes Profondes de l'Atlantique Oriental Tropical. Par A. Crosnier et J. Forest. Pp. 408. (Paris et Bondy: Office de la Recherche Scientifique et Technique Outre-Mer, 1972 et 1973.) [289]

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SCHOOL OF CHEMICAL ENGINEERING

High academic qualifications in chemical engineering or related fields required, together with experience in plant and process design or instrumentation and control. Experience in the oil or gas industries advantageous. Applications close March 29, 1974.

SCHOOL OF CHEMICAL ENGINEERING (FOOD TECHNOLOGY)

High academic qualifications in food science or microbiology required. Experience in food microbiology or related field highly desirable. Successful applicant will teach food microbiology at both graduate and undergraduate level. Applications close March 29, 1974.

SCHOOL OF MATHEMATICS

In field of applied mathematics. Teaching and research experience in control theory, game theory, or some allied mathematical applications in industry or commerce preferred. Applications close January 18, 1974.

Salary: \$A8,698 range \$A11,982 per annum. Commencing salary according to qualifications and experience.

For details of appointment, including superannuation, study leave and housing scheme, write to the Secretary-General, Association of Commonwealth Universities (Appis), 36 Gordon Square, London WC1H 0PF. (2029)

ALFRED HOSPITAL

COMMERCIAL ROAD, PRAHRAN, VIC. 3181
AUSTRALIA

Applications are invited from suitably qualified persons for appointment to the position of:

DEPUTY DIRECTOR OF BIOCHEMISTRY

Applicants should be graduates in Medicine or Science and should preferably have an appropriate higher qualification. Experience in the organisation of a hospital biochemistry service and knowledge of the role of biochemical investigation in the care of patients is essential.

Alfred Hospital is a large teaching hospital and is affiliated with Monash University. The Biochemistry department has a staff of thirty (30) people and is well equipped with a wide range of equipment including computerised auto-analysers. The department is moving, in early 1975, to new laboratories, and at that time the range of instrumentation will be extended considerably.

Commencing salary, depending upon qualifications and experience, will be within the following ranges:
Medical Graduate, \$15,069.60 to \$20,706.40 per annum;

Science Graduate, \$13,774.28 to \$15,701.40 per annum.

Superannuation is available.

Further details may be obtained from the Director, Dr. M. Briggs.

Applications close on January 21, 1974, and are to be submitted on forms obtainable from the undersigned.

G. B. CANHAM,
Manager
(2042)

CSIRO

DIVISION OF FISHERIES AND OCEANOGRAPHY CRONULLA, N.S.W.

AUSTRALIA

RESEARCH SCIENTIST

The Commonwealth Scientific and Industrial Research Organisation has a broad charter for research into primary and secondary industry areas. The Organisation has approximately 6,500 employees—2,100 of whom are research and professional scientists—located in Divisions and Sections throughout Australia.

FIELD: MARINE ZOOBENTHOS

GENERAL: The Division has a staff of over 40 scientists investigating the fisheries resources and the physical, chemical and biological features of the oceans. Headquarters of the Division is located at Cronulla, Sydney, and the Division has laboratories in Perth and near Brisbane. The appointee will be located at Cronulla.

An ecosystems group is currently working with physicists and chemists in the Division on an interim study of a deep water body within Port Hacking, a flooded valley system subject to periodic deoxygenation. Later studies could involve completely different systems elsewhere in Australia. Aquarium and seawater facilities are available. Extensive provision for use of computer facilities has been made.

DUTIES: To join an interdisciplinary group of ecologists carrying out collaborative studies on selected marine ecosystems. The present emphasis is on estuaries and shallow seas. To develop a research programme on some aspect of the biology of zoobenthos communities, with particular relevance to their functional relationship to ecosystems as a whole, and to collaborate with colleagues in modelling the study systems.

QUALIFICATIONS: A Ph.D. degree in zoology or equivalent qualifications, together with demonstrable research ability. Considerable experience in animal ecology, preferably on marine zoobenthos or some closely related field in marine biology would be an advantage.

SALARY: The appointment will be made within the salary ranges of Senior Research Scientist or Principal Research Scientist: \$A12,298–\$A17,077 p.a.

TENURE: An indefinite or a three year fixed term appointment may be negotiated. An indefinite appointment carries Australian Government Superannuation benefits.

Applications stating full personal and professional details, the names of at least two professional referees, and quoting Reference Number 320/508 should reach:

The Personnel Officer,
Australian Scientific Liaison Office,
64–78 Kingsway, LONDON WC2B 6BD.

by the 25th January, 1974.

Applications in U.S.A. and Canada should be sent to
The Counsellor (Scientific),
Embassy of Australia, 1601 Massachusetts Avenue, N.W.,
WASHINGTON, D.C. 20036, U.S.A.

(2086)

UNIVERSITY OF EDINBURGH

DEPARTMENT OF MATHEMATICS

LECTURESHIPS IN PURE AND APPLIED MATHEMATICS

Applications are invited for TWO LECTURESHIPS in either Pure or Applied Mathematics tenable from October 1, 1974.

Salary scale: £1,929 to £4,548 per annum. Applications, by letter (one copy), together with a curriculum vitae and the names of at least two referees, should be sent to the Secretary to the University, University of Edinburgh, Old College, South Bridge, Edinburgh EH8 9YL, from whom further particulars may be obtained.

The closing date for applications is January 21, 1974. Please quote Reference 1072.

(2030)

AGRICULTURAL RESEARCH COUNCIL POULTRY RESEARCH CENTRE

Applications are invited for a SCIENTIFIC OFFICER post at the Poultry Research Centre's Outstation, Roslin, Midlothian. The duties will initially be to assist scientific and farm staff in the artificial insemination of turkeys and other general duties.

Qualifications: Pass degree, H.N.C. or equivalent in the field of animal husbandry. Salary: Within the scale £1,318 to £2,177 per annum, with placement according to qualifications and experience. The post is superannuable with a non-pensionable allowance to offset contributions.

Application forms, which may be obtained from the Secretary, Poultry Research Centre, King's Buildings, West Mains Road, Edinburgh EH9 3JS, should be completed and returned to him not later than January 10, 1974.

(2031)

British Museum (Natural History)

Zoologist

- Curatorial and advisory work in Mollusca Section
- Opportunity for taxonomic research on selected groups.

☐ 1st/2nd hon's degree or equivalent in Zoology or Geology
☐ At least two years postgraduate experience ☐ Age under 32 ☐ Appointment as Senior Scientific Officer (£2790-£3815) or Higher Scientific Officer (£2251-£2842) ☐ Ref: SB/14/DK ☐ Closing date 11 January 1974.
☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Ministry of Agriculture, Fisheries and Food
 Food Science Division, London

Food Chemist/ Biochemist

- Advise on scientific aspects of manufacture and composition of foods and beverages
- Liaise with other Government Departments
- Participate in committee work in UK and abroad and in current awareness studies.

☐ 1st/2nd honours degree in Food Science/Technology or related science ☐ At least 4 years postgraduate experience in food industry or research on meat, fish, milk or protein foods ☐ Age 26-32 ☐ Appointment as Senior Scientific Officer (£2790-£3815) ☐ Ref: SB/5/AE ☐ Closing date 11 January 1974.
☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Centre for Overseas Pest Research
 Pesticide Residues Group

Biologist

- Co-ordinate research and advisory work on effects of pesticide residues in tropical soils
- Considerable work overseas, including participation in training schemes.

☐ 1st/2nd hon's degree or equivalent in Biology ☐ Knowledge of tropical soil ecology ☐ Age 26 to 31 ☐ Appointment as Senior Scientific Officer (£2790-£3815) ☐ Ref: SA/7/JA ☐ Closing date 11 January 1974.
☐ Application forms from the Administrative Secretary, Centre for Overseas Pest Research, College House, Wrights Lane, London W8 5SJ.

Ministry of Agriculture, Fisheries & Food
 Food Science Division, London.

Chemist/Biochemist

- Organise surveys of processing and environmental contamination effects on safety and nutritional value of food
- Liaise with other bodies engaged in food monitoring
- Report findings to committees and working parties
- Participate in committee work.

☐ 1st/2nd hon's degree in Chemistry, Biochemistry or related science ☐ At least 4 years postgraduate experience ☐ Age 26-31 ☐ Appointment as Senior Scientific Officer (£2790-£3815) ☐ Ref: SB/6/AE ☐ Closing date 11 January 1974.
☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24 hour answering service).

Department of Agriculture and Fisheries for
 Scotland Agricultural Scientific Services,
 East Craigs, Edinburgh

Botanist/Biologist

- Assist with trials to determine the distinctness, field performance and consumer quality of new varieties of potato
- Carry out laboratory and glass-house tests on disease susceptibility of potatoes
- Some field and ad hoc experimental work.

☐ Degree or equivalent in Botany, Agriculture or Biology. ☐ Age under 27 ☐ Appointment as Scientific Officer (£1318-£2177) ☐ Ref: SA/2/DLA ☐ Closing date 11 January 1974.
☐ Application forms from Scottish Office, Personnel Division, Room 172, St. Andrew's House, Edinburgh EH1 3BX, telephone 031-556 8501 ext 2621.

Department of Health and Social Security
 British Pharmacopoeia Commission, London

Chemists/ Pharmacists

- Secretarial and editorial work for British Pharmacopoeia
- Collection of data from technical journals, foreign pharmacopoeia for reports to committees
- Assist in work for European Pharmacopoeia.

☐ Degree in Chemistry or Pharmacy or HNC in Chemistry ☐ Practical experience in quality control an advantage ☐ Age under 30 ☐ Appointment as Higher Scientific Officer (£2251-£2842) or Scientific Officer (£1493-£2352) ☐ Ref: SB/2/KD ☐ Closing date 11 January 1974.
☐ Application forms from Civil Service Commission, Alencon Link, Basingstoke, Hants RG21 1JB, telephone Basingstoke 29222 ext 500 or London 01-839 1992 (24-hour answering service).

**Science
group**
 CIVIL SERVICE

(2050)

ABSTRACTORS/TRANSLATORS

Graduates in microbiology, biochemistry or allied subjects with a good knowledge of either French or German are required for full-time abstracting work.

Please apply to: Dr. E. S. Krudy, Information Retrieval Limited, 1 Falconberg Court, London W1V 5FG. (2092)

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 small M.R.C. team working on the development and behaviour of the avian embryo, including its capacity to receive and transmit signals. We want a research worker who will make use of his basic knowledge to help solve our problems. Some aptitude for electronics essential. Medical Research Council scales. F.S.S.U.—Inquiries to Margaret A. Vince, Psychological Laboratory, Downing Street, Cambridge CB2 3EB. (1856)

ABTRACTOR

A graduate in microbiology, biochemistry or allied subjects is required for full-time abstracting work.

Please apply to: Dr. E. S. Krudy, Information Retrieval Limited, 1 Falconberg Court, London W1V 5FG. (2091)

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Organon is an ethical drug manufacturer with research facilities in the Netherlands and abroad.

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Candidates must have obtained their M.D. or Ph. D. degree within the last three years. Duration of fellowships is minimally 12 months with the possibility of extension. Financial arrangements depend on age and training of candidates and will be approximately in line with current academic remuneration in Holland.

As English is the official company language, fluency in English is essential.

There are no restrictions re age, sex or nationality. Candidates will be preselected on the basis of

their curriculum vitae and two letters of recommendation by professors of their own choice. Those interested are requested to apply to Dr. H. G. Wijmenga, Head Research and Development Laboratories, Organon International BV, P.O. Box 20-Oss, Netherlands.



Organon International BV
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(2064)

European Molecular Biology Organization (EMBO)

Short- and long-term fellowships in molecular biology

The European Molecular Biology Organization intends to award to scientists working in laboratories within the European area both short-term (from a few days to several weeks) and longer-term fellowships for collaborative research or advanced training in molecular biology.

The Short-term Fellowships are to support visits to other laboratories for the purpose of carrying out experiments with special techniques or of other forms of scientific collaboration or advanced training, and especially to support developments arising at short notice.

The Long-term Fellowships will usually be for a period of one year, but applications for renewal will be considered. They will be awarded upon individual application, at the "junior" level to promising young research workers who may then spend prolonged periods in other laboratories working under the guidance of leaders in the field of molecular biology. At the "senior" level, they may be awarded to enable established research workers to gain experience in new approaches and new problems. Upon application by European Institutions fellowships at the "senior" level may also be awarded to specialists who can assist in the initiation and development of research programmes in the sponsoring Institution. Such "sponsored" awards may be made to established workers at all stages of their career beyond the postdoctoral stage.

Application forms and further details may be obtained from Dr. J. Tooze, Executive Secretary, European Molecular Biology Organization, 6900 Heidelberg 1, Postfach 2029 (Postfach 1022.40 after July 1, 1974), Germany.

Application for Short-term Fellowships may be made at any time and will be decided upon soon after receipt of the application. Applications for Long-term Fellowships should be made before February 1 for a decision by April 30 and before August 1 for a decision before October 31. Because the selection procedure involves an interview these deadlines for application should be respected.

(X1822)

UNIVERSITY OF MANCHESTER

TURNER AND NEWALL RESEARCH FELLOWSHIP

Applications invited for one Fellowship, founded by Turner and Newall Limited, available for post-doctoral research in Chemistry, Physics, Geology, Mineralogy, Metallurgy, Applied Mathematics, Engineering, Medicine and allied subjects. Tenable from October 1, 1974, for two years. Salary range: £1,560 to £1,768 per annum. F.S.S.U.

Particulars and application forms (returnable by January 8, 1974) from the Registrar, The University, Manchester M13 9PL. Quote ref: 204/73/N.

(2037)

THE QUEEN'S UNIVERSITY OF BELFAST

S.R.C. RESEARCH STUDENTSHIPS

The Science Research Council is likely to offer to suitable candidates a limited number of Research Studentships for 1974 tenable in the Faculties of Science or Applied Science and Technology; the former includes the Departments of Pure Mathematics, Applied Mathematics and Theoretical Physics, Statistics and Operational Research, Computer Science, Pure and Applied Physics, Analytical, Inorganic, Organic, Physical and Industrial Chemistry, Biochemistry, Zoology, Botany, Psychology, Archaeology and History and Philosophy of Science; the latter, Engineering Mathematics, Civil, Mechanical, Electrical and Aeronautical Engineering Departments.

The value of these will be in accordance with S.R.C. scales, and students graduating in 1974 in Great Britain (and who are not resident in Northern Ireland) are invited to write, stating their particular field of interest, to the Dean of the selected Faculty by Tuesday, January 8, 1974.

(2033)

AUSTRALIAN INSTITUTE OF NUCLEAR SCIENCE
& ENGINEERING

A.I.N.S.E. Research Fellowships

ANNOUNCEMENT

A.I.N.S.E. Research Fellowships are offered by the Australian Institute of Nuclear Science and Engineering for suitably qualified persons wishing to undertake research projects within the Institute's field of interest. Candidates for these awards must be nominated by an Australian University or the Australian Atomic Energy Commission. The closing dates are February 28 and August 31 each year, and all nominations received by the Institute after one closing date, will be considered together after the next closing date.

Research Fellowships are intended for scientists and engineers who have qualifications equivalent to the Degree of Ph.D. and are at a relatively early stage of an independent research career. Minimum tenure is two years, and the award may be extended for a third year. Emolument will be within the range of \$8,000 per annum to \$11,000 per annum (Australian currency), and the Institute may contribute to the costs involved in travelling to and from Australia.

A research project within the field of nuclear science and engineering of interest to the Institute may be proposed in the nomination after agreement between the candidate and the nominating organisation. Usually it is expected that a Research Fellow's project will require some use of the specialised facilities located within the Australian Atomic Energy Commission Research Establishment at Lucas Heights, near Sydney, N.S.W.

Further information may be obtained from:

The Executive Officer,
Australian Institute of Nuclear Science and Engineering,
Private Mail Bag,
Post Office,
Sutherland, N.S.W. 2232,
Australia.

(2067)

MEETING

Microtubules and Microfilaments

A meeting on Microtubules and Microfilaments, sponsored by the European Molecular Biology Organisation, will be held in Gargnano, Lake Garda, Italy, on May 12-15, 1974.

Post-doctoral and postgraduate research workers and other interested persons should apply to Dr. A. C. Allison, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ. Expenses for accommodation will be provided and limited travel funds are available. (2082)

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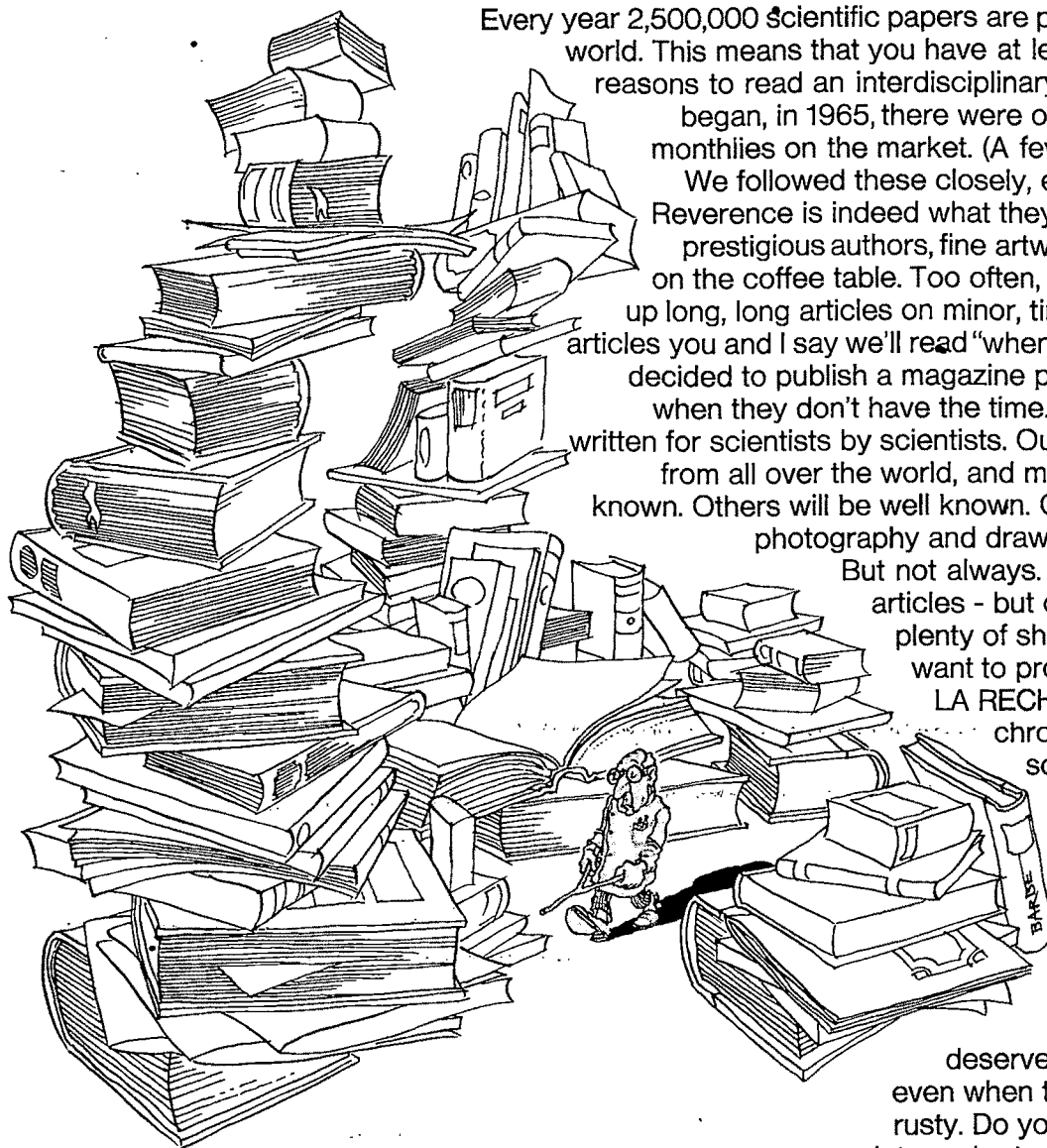
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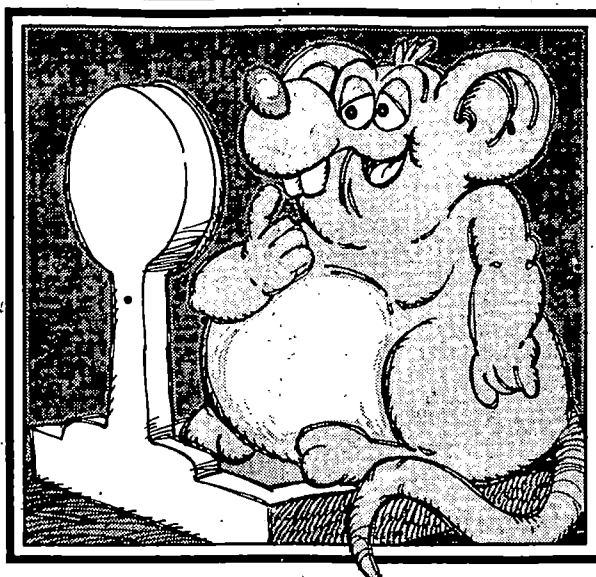
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